

Official Publication of The American Federation for Clinical Research

Clinical Research Proceedings

VOL. I, NO. 2

SEPTEMBER, 1953

IN THIS ISSUE

ABSTRACTS submitted to the NATIONAL MEETING of the
American Federation for Clinical Research,
Atlantic City, May 1953, *page 61*

NOTICES of Importance to Investigators, *page 118*

MEMBERSHIP ROSTER, American Federation for
Clinical Research, *page 121*

ANNUAL AUTHOR INDEX, *page 144*

ANNUAL SUBJECT INDEX, *page 148*

Published by Grune & Stratton, Inc.

Abstracts Submitted to the Annual
National Meeting
of the
American Federation for Clinical Research

Steel Pier Theater, Atlantic City, New Jersey • Sunday, May 3, 1953

BLOOD

Iron Metabolism • Anemias • Leukocytes • Immunohematology Blood Clotting and Anticoagulants

The Relationship of Plasma Iron to the Kinetics of Iron Metabolism. *Stuart C. Finch and Joseph F. Ross*, Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine, Boston.

Changes in the quantity and speed of iron exchanged between its plasma and tissue compartments have been studied in animal and human subjects in order to delineate more clearly the relationship between plasma iron and total body iron. Following intravenous administration of tracer amounts of radioactive iron to 59 subjects, the plasma iron turnover rate (quantity of iron exchanged per unit time) and plasma iron clearance rate (speed of exchange) were determined and correlated with alterations in hematopoietic rates, plasma and total body iron concentrations, and the integrity of the reticuloendothelial tissue. These studies indicate that with alterations in the quantity of total body iron, the changes in plasma iron concentration correlate well with plasma iron clearance, but neither is a reliable index of the hematopoietic rate. The plasma iron turnover reflects more closely the true hematopoietic rate, but the quantity of iron exchanged invariably is in excess of that required for hemoglobin synthesis. Even in the presence of severe iron depletion with restriction of hemoglobin synthesis, appreciable amounts of iron continue to exchange between the plasma and iron storage depots. In the presence of tissue iron excess, iron turnover outside the hemoglobin cycle is greatly increased. Plasma iron turnover studies on dogs following acute blood loss indicate that tissue iron for hemoglobin synthesis is mobilized several

days before any appreciable reticulocyte response is apparent. Functional integrity of the reticuloendothelial system has been shown to be important in the regulation of iron exchange between tissue and plasma.

A Comparison of C^{14} , Fe^{59} , and Ashby Technic for Determination of Red Cell Life Span. *N. I. Berlin, M. L. Beeckmans,* P. J. Elmlinger* and J. H. Lawrence*, Donner Laboratory, University of California, Berkeley.

Three methods in use for determining life span of red cells are the Ashby differential agglutination, radioactive iron to measure rate of red cell production and long-term Fe^{59} uptake curves, and the use of N^{15} - and C^{14} -labeled glycine for the labeling of hemoglobin. Of the three, the last rests upon the firmest foundations. However, since all methods are being used, comparative data are needed.

Four patients were studied by all methods. In 3 patients with lymphomatous disease, all technics gave comparable results, showing a slight decrease in the red cell life span. In a patient with secondary polycythemia, the Ashby technic showed a random destruction, with 50% destruction in 36 days, while calculation of the life span from Fe^{59} red cell production rate gave 86 days and from the Fe^{59} red cell content method gave 105 days. Finally, the C^{14} -glycine method showed 100 days; and the iron and C^{14} methods showed finite life spans. In 9 other patients, simultaneous radioiron and C^{14} measurements gave similar results in 5, and discrepancies were noted in four.

*An asterisk indicates "by invitation."

When the red cell life span is in the normal range, all methods yield similar results, but when there is an alteration in red cell life span, significant differences are obtained by the three methods. The relation of these results to the mechanism of the anemia in leukemia will be discussed.

Evidence Favoring a Humoral Mechanism for Anoxemic Polycythemia. *Frederick Stohlman, Jr., Charles E. Rath and John C. Rose*, Department of Medicine, Georgetown University Hospital and the Georgetown University School of Medicine, Washington, D. C.

A direct effect of anoxia on the bone marrow has been postulated by some as the cause of erythrocytosis secondary to anoxemia. Other investigators suggest that a lowered arterial O_2 tension stimulates the production of a humoral substance capable of inducing erythrocytic hyperplasia but that low O_2 tension by itself is unfavorable for erythropoiesis.

Studies have been completed on a patient with polycythemia secondary to a patent ductus arteriosus with reversal of flow as a result of pulmonary hypertension. This unusual condition produced cyanosis confined to the lower half of the body. The diagnosis was confirmed by cardiac catheterization, which revealed a mean pulmonary artery pressure of 102 mm. Hg and a mean systemic arterial pressure of 96 mm. Hg. Hematologic values were: Hematocrit 62; white blood count, 7,040; platelets, 154,000; total blood volume ($T 1824 + Cr^{51}$), 3590 cc.; red cell mass (Cr^{51}), 43.5 cc./Kg. Hemolytic studies were negative in result. There was marked erythrocytic hyperplasia of the sternal marrow with a shift toward immaturity. The iliac marrow was repeatedly hypoplastic, with a decreased M:E ratio. Simultaneous O_2 saturations were: Femoral artery 47%; brachial artery 92%; sternal marrow 69%; iliac marrow 42%. Further studies on peripheral and marrow blood O_2 and pH have confirmed the observation that the sternal marrow is adequately oxygenated while the iliac marrow is anoxic.

These data indicate that erythropoietic activity may be suppressed by localized low O_2 tension, while in the same patient, red cell hyperplasia, sufficient to produce polycythemia, exists in areas where O_2 tension is normal. This is thought to favor a humoral mechanism for anoxemic polycythemia.

Severe Iron-Deficiency Anemia in an Adolescent Male. *William J. Grace and Ralph L. Engle, Jr.,** Departments of Medicine and Psychiatry, New York Hospital-Cornell Medical Center, New York.

Severe degrees of iron-deficiency anemia in adolescent women have long been recognized in clinical medicine and, indeed, chlorosis was once a major problem. However, severe degrees of iron-deficiency anemia in adolescent males have always been rare. A 13 year old male with a severe iron-

deficiency anemia presented an opportunity to study iron metabolism in this situation. Absorption of iron from the gastrointestinal tract was studied and compared with absorption of iron in healthy persons. Six such studies were made and one study of the absorption of radioactive iron was also carried out. In each of these determinations, the absorption of iron was impaired as compared to absorption of iron in a group of healthy persons. The patient responded rapidly to the administration of intravenous iron. It is felt that the poor iron absorption in this person was a sufficient explanation for the severe iron-deficiency anemia.

Simultaneous Paper Electrophoresis of Large Numbers of Hemoglobin Samples in the Rapid Screening of Populations for Asymptomatic Heterozygous Carriers of Certain Abnormal Hemoglobins. *William Q. Wolfson and James V. Neel*, Rackham Arthritis Research Unit, Department of Internal Medicine, and the Heredity Clinic, Institute of Human Biology, University of Michigan, Ann Arbor.

Two major peaks are seen in electrophoretic patterns of hemoglobin from heterozygous carriers of sickle cell gene and hemoglobin C gene. One peak is the characteristic abnormal hemoglobin; the other, normal hemoglobin. Electrophoresis is unimportant in detecting sickle cell trait carriers because this differentiation is effectively and more simply accomplished by induced sickling tests. However, heterozygous hemoglobin C carriers show no characteristic hematologic findings comparable to induced sickling, and demonstration of the typical electrophoretic pattern is essential for diagnosis. For rapid screening in genetic or diagnostic studies, apparatus has been developed to permit simultaneous study of 50 or more samples by paper electrophoresis (Zenith Plastics). Native hemoglobins appear satisfactory. Hemolyzed samples diluted with buffer (pH 8.4 to 8.9 veronal, 0.045 M in sodium veronal with 10% added ethanol) are exhaustively centrifuged at over 10,000 rpm to insure complete removal of stroma. Samples are run at 7.5 to 20.0 volts per linear inch on large sheets of Munktell 20B paper fully equilibrated with buffer before spotting. Direct inspection usually suffices for diagnosis. Alternatively, patterns may be stained for protein with bromphenol blue or Bioblue (resembles Amidoschwarz 10B) or, more specifically, for hematin with the highly sensitive benzidine-peroxide reagent (Quastel and Franklin). Quantification may be accomplished either by spot elution or direct photometric scanning of stained patterns. Careful attention to many technical factors is an absolute requirement for optimum results.

The Differentiation of Various Types of Sickle Cell Disease by Paper Electrophoresis of Hemoglobin. *Rose G. Schneider** (introduced by William C.

Levin), Tissue Metabolism Research Laboratory and Tissue Culture Laboratory, University of Texas Medical Branch, Galveston.

A convenient, inexpensive apparatus for paper electrophoresis of human hemoglobin has been constructed. This apparatus permits the analysis of as many as 12 hemoglobin samples simultaneously. The procedure is rapid and simple, since advantage is taken of the hemoglobin color and no staining is required. Within 2 to 3 hours, it provides a clear differentiation between hemoglobin from normal subjects and that from patients with sickle cell anemia or sickle cell trait. In a run of 3 to 6 hours, the presence of the recently described hemoglobin C may be determined.

When artificial mixtures of normal and sickling hemoglobin are prepared in varying proportions, it is possible to detect as little as 10% of one of these types of hemoglobin in the presence of 90% of the other. By comparing an unknown sample with several known mixtures, an approximate estimation of the percentage of each type of hemoglobin is obtained.

This method offers a reliable diagnostic procedure to differentiate patients with sickle cell anemia from those with sickle cell trait and an unrelated anemia, as well as to differentiate both of these conditions from the type of sickle cell disease in which sickling hemoglobin is combined with hemoglobin C.

This method is currently being used to correlate the hemoglobin content of erythrocytes of patients with sickle cell disease with their immunologic characteristics and to determine the incidence of hemoglobin C. Another useful application is to the genetic study of families with sickle cell disease. The hemoglobin samples of all the members of a family are analyzed simultaneously on one piece of filter paper, producing a permanent pictorial record of the types and relative concentrations of each type of hemoglobin in every member of the family.

Hemodynamic Studies in Sickle Cell Anemia. Leonard Leight,* Thomas H. Snider,* George O. Clifford* and Harper K. Helms, Wayne University College of Medicine, Detroit.

Thirteen patients with sickle cell anemia, varying in age from 12 to 39 years and with hemoglobins varying from 5.81 to 10.77 Gm., have been studied at rest and during exercise by means of cardiac catheterization. Cardiac dilatation and/or hypertrophy was present in all, and left auricular enlargement in 4. All patients had systolic murmurs, and 3 an apical diastolic murmur.

Cardiac index at rest varied from 5.16 to 7.6 L./min./M². Despite the high resting output and the long standing anemia, there was a significant increase in cardiac output with exercise in the majority of patients. The pulmonary vascular pressures were normal, both at rest and during exercise, in 7

of the 13 patients. Four patients with normal pulmonary artery pressure at rest showed an increase in pressure with exercise, associated in 2 with a rise in pulmonary capillary pressure. One patient had the pattern of cor pulmonale with a pulmonary artery pressure of 49/26 mm. Hg and a pulmonary capillary mean pressure of 7 mm. Hg. One patient had hemodynamic findings consistent with a diagnosis of mitral stenosis.

Low arterial oxygen saturation, varying from 77.3 to 92.8%, was found in 7 of the 13 patients catheterized, and in 12 of 13 patients studied by arterial puncture only. None of these patients had clinical or roentgenologic evidence of pulmonary disease, with the exception of the case of cor pulmonale. Studies are in progress correlating the electrophoretically determined type of hemoglobin with the oxygen saturation in patients with sickle cell anemia and trait.

The Clinical and Hematologic Characteristics of Sickle Cell-Hemoglobin C Disease and the Hemoglobin C Trait. Eugene Kaplan,* James V. Neel, and Wolf W. Zuelzer,* Children's Hospital of Michigan, Detroit, and Institute of Human Biology, University of Michigan, Ann Arbor.

Occurrence of an inherited abnormality of hemoglobin, termed hemoglobin C, has been recognized in American Negro families as a result of clinical, genetic, and physicochemical studies of individuals with atypical forms of sickle cell disease. Hemoglobin C may be identified by its characteristic electrophoretic behavior. Family studies indicate that the presence of the hemoglobin is due to a single dominant gene. Individuals heterozygous for the hemoglobin C gene alone exhibit an asymptomatic carrier state, the hemoglobin C trait. However, the combination of the genes responsible for sickle cell hemoglobin and hemoglobin C results in a mild hemolytic syndrome, sickle cell-hemoglobin C disease.

An attempt has been made to arrive at a precise clinical and hematologic definition of these two conditions which will permit their recognition by simple hematologic methods. Sickle cell-hemoglobin C disease has a characteristic clinical and hematologic profile distinct from that of sickle cell anemia. The clinical course is relatively benign, and there is a mild hemolytic anemia with erythrocyte sickling and very numerous target cells. Only one parent of these individuals has the sickle cell trait, while the nonsickling parent is a carrier of hemoglobin C. The hemoglobin C trait has now been studied in 14 individuals. The condition is entirely asymptomatic and an increase in target cells is the only consistent hematologic abnormality. It is clearly differentiated from the sickle trait by an absence of sickling, and from thalassemia minor by an absence of microcytosis and hypochromasia.

Hematologic Studies on Patients with Sickle Cell Anemia following Multiple Transfusions of Whole Blood. Charles C. Donegan* and Byrd S. Leavell, Department of Internal Medicine, School of Medicine, University of Virginia Hospital, Charlottesville.

Six patients with sickle cell anemia were transfused with normal whole blood of the same type at intervals of one or two days. The erythrocyte counts reached normal in a period of 8 days or less, at which time transfusions were discontinued. Erythrocyte, reticulocyte, sickled erythrocyte, plasma bilirubin, and fecal urobilinogen values were determined at regular intervals for several weeks. The results were similar in all patients. Absolute values of both reticulocytes and sickled erythrocytes in the circulating blood fell rapidly. Within 7 to 10 days after the first transfusion, both reticulocytes and sickled erythrocytes were but a fraction of the original values. Plasma bilirubin and fecal urobilinogen excretion decreased in a more gradual fashion. Within 30 days, as the total erythrocyte count began to fall, reticulocytes, sickled erythrocytes, and plasma bilirubin again increased.

Our interpretation of these observations is that the production of a normal erythrocyte count in the peripheral blood caused a prompt depression of erythropoiesis. As a result, the production of sickled erythrocytes was reduced markedly. In such circumstances the number of these cells in the peripheral blood diminished rapidly because of their short life span. Since the clinical manifestations of sickle cell anemia appear to result from anemia and also from sickling of the erythrocytes in the capillaries, the data suggest that multiple transfusions may be a means of reducing the number of complications that occur in patients with sickle cell anemia during pregnancy, delivery, and anaesthesia.

Red Cell Life Span in Hereditary Ovalocytosis.

Arno C. Motulsky,* Karl Singer,* William Crosby* and Vernon Smith* (introduced by Milton H. Paul), Department of Hematology, Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington, D. C., and the Department of Hematologic Research, Michael Reese Research Institute, Chicago.

Differential agglutination studies with red cells from 3 unrelated patients with hereditary ovalocytosis revealed normal survival time of the ovalocytes in 2 instances. The red cells from a third patient with the condition showed a diminished survival time of 45 days. This patient was not anemic but had an elevated hemolytic index (30), elevated reticulocyte count (3.2%) and borderline serum bilirubin (1 mg. %). These findings were interpreted as evidence of a "compensated hemolytic syndrome." Since 2 recipients were children with sickle cell anemia, the life span of the abnormal cells could also be roughly estimated by observing the dis-

appearance of the nonsickling ovalocytic cells in sickle cell preparations. A recent claim of shape transformations of ovalocytes into normocytes during the latter portion of their life span could not be confirmed.

These findings point out that some cases of hereditary ovalocytosis may be instances of an intracorporeal hemolytic syndrome. Morphologically, ovalocytes with normal life span are indistinguishable from functionally defective ovalocytes. Hereditary ovalocytosis thus resembles Mediterranean disease where mild forms of the condition are associated with normal life span while the severe disease shows diminished survival.

Dynamics of Erythropoiesis and Cell Survival Studied with N^{15} -Glycine during Therapeutic Remission in Megaloblastic Anemias. G. Watson James, III, and Lynn D. Abbott, Jr.,* Laboratory for Clinical Investigation, Department of Medicine and Department of Biochemistry, Medical College of Virginia, Richmond.

The dynamics of hemoglobin synthesis and the survival of erythrocytes formed during reticulocytosis in therapeutically induced remissions were studied in 3 patients with pernicious anemia, one with megaloblastic anemia secondary to total gastric resection, and one with megaloblastic anemia of sprue. On the day of maximum reticulocytosis following parenteral vitamin B_{12} or oral folic acid (sprue patient only), two 500 mg. doses of N^{15} -glycine (31 atom % N^{15}) were given orally three hours apart. Incorporation of heavy nitrogen into the heme of hemoglobin and its subsequent disappearance were determined by hemin isolation and analysis. In all patients maximum incorporation of N^{15} had occurred 8 days later ($18-20 \times 10^{-4}$ meq. heme N^{15} per 100 ml.). Uptake in 2 nontreated normal adult males was very small (4×10^{-4} meq. heme N^{15} per 100 ml.).

It was possible to follow the patients with sprue and total gastric resection for 165 days. Decrease in hemin N^{15} concentration occurred in two phases. Initial rapid fall from the 8th to the 40th day was interpreted as due primarily to dilution of the labeled cells with newly-formed nonlabeled erythrocytes. A short plateau followed, then a second slower phase began about the 80th day and was due to increased destruction of the tagged cells with age. Average life span of the cells in each patient was about 114 days.

The erythrocytes produced under the stimulus of rapid erythropoiesis had a normal life span. At the time of maximum reticulocytosis, marked incorporation of N^{15} into hemoglobin occurred with very small amounts of labeled glycine.

Studies of Prothrombin Concentration in Patients with Pernicious Anemia Treated with Vitamin B_{12} . Gunnar Vetne,* Arnold Axelrod and Shirley

A. Johnson,* Wayne University, College of Medicine, Detroit.

There is general agreement that hypoprolthrombinemia is a rather constant finding in patients with pernicious anemia in relapse. There are conflicting reports in the literature concerning the effect of vitamin B₁₂ therapy on this deficiency.

In our studies prothrombin concentration was determined in 40 patients with pernicious anemia treated with vitamin B₁₂. All patients were in remission and had received B₁₂ for more than 2 years. In all patients, prothrombin determinations were done by the methods of Quick, Owren, and Ware and Seegers. Approximately 50% of the cases showed significant reduction in prothrombin concentration determined by Owren's method and the two-stage method of Ware and Seegers. The results of these two methods showed good correlation. Quick's method, on the other hand, revealed no correlation and gave normal results in almost all patients. Proconvertin (SPCA) was also determined using the one-stage technic of Owren. In most cases in which there was prothrombin deficiency, proconvertin was also reduced. Standard liver function tests failed to reveal any correlation between the concentration of prothrombin and liver function.

In conclusion, using Owren's method and the two-stage method of Ware and Seegers, we have demonstrated hypoprolthrombinemia in many of our patients with pernicious anemia treated with vitamin B₁₂. Quick's method is too insensitive to record this deficiency.

Inhalation and Nasal Instillation of Crystalline B₁₂ Therapy in Pernicious Anemia. *Raymond W. Monto, John W. Rebeck* and Michael J. Brennan*, Division of Hematology and Department of Laboratories, Henry Ford Hospital, Detroit.

Eight cases of pernicious anemia in relapse were treated with vitamin B₁₂ by inhalation or nasal instillation. Three of these patients received crystalline B₁₂ in physiologic saline without a preservative by vaponephrin nebulizer. B₁₂ lactose powder was administered to one patient by a dust inhalator. Nasal instillation of vitamin B₁₂ in saline was utilized in the last 4 cases. Twenty patients with pernicious anemia in remission were given inhalation B₁₂ therapy at comparable intervals to maintenance parenteral treatment. Inhalation, nasal instillation, and direct administration of B₁₂ into the pulmonary tree by means of a bronchoscope produced urinary excretion of detectable amounts of the material. Mucous membrane irritation and sensitization have not been encountered to date.

Inhalation and nasal instillation of crystalline vitamin B₁₂ in saline and lactose powder have produced satisfactory clinical and hematologic responses in 8 patients with pernicious anemia in relapse. Twenty patients with pernicious anemia in remission

have been maintained by inhalation B₁₂ technics for periods up to one year.

Vitamin B₁₂ in Blood and Urine of Three Patients with Pernicious Anemia during Oral Treatment with Vitamin B₁₂ Combined with Intrinsic Factor Concentrate from Hog Stomach Mucosa. *George B. Jerzy Glass, and Lois C. Lillick* and Linn J. Boyd,** Departments of Medicine and Bacteriology, New York Medical College, Flower and Fifth Avenue Hospitals, New York. (This investigation was supported by a Research Grant from the National Institute of Arthritis and Metabolic Diseases of the National Institute of Health, Public Health Service.)

In 3 patients with pernicious anemia in relapse, vitamin B₁₂ was determined in the blood and urine by *E. coli* mutant assay during 3.5 to 5.5 weeks of oral treatment with vitamin B₁₂ combined with intrinsic factor concentrate from hog stomach mucosa. Urinary outputs of vitamin B₁₂ were correlated with hematopoietic responses, as determined by daily counts of reticulocytes, erythrocytes and hematocrit.

During the entire period of oral treatment urinary and blood serum concentrations of vitamin B₁₂ were most frequently below 0.2 µg./ml., i.e., below the lowest range detectable with the technic used. Only occasionally did they rise to 0.4-0.6 µg./ml. The daily urinary outputs were 0.5-1.5% of the ingested dose, and below 2%, if the undetectable amounts of B₁₂ were also included in the calculations. Since the hematopoietic responses indicated that at least 6% of the dose ingested was absorbed, the inference was drawn that only one part of orally absorbed vitamin B₁₂ was excreted in the urine in microbiologically active form.

When 1000 µg. vitamin B₁₂ was given orally alone or together with a potent intrinsic factor concentrate, only 1/6,000-1/9,000th of the dose ingested was recovered in the urine. The hematopoietic response produced under these circumstances indicated that much more vitamin B₁₂ was absorbed than excreted in the urine. This suggested some binding and retention of vitamin B₁₂ in the body following its intestinal absorption, or possibly some metabolic change resulting in the loss of microbiologically detectable activity. A significant increase of urinary excretion of vitamin B₁₂ was observed in all 3 cases of pernicious anemia treated orally with vitamin B₁₂ immediately following the hematopoietic response, and especially the rise in reticulocytes.

Oral Treatment of Pernicious Anemia with Small Doses of Vitamin B₁₂ Combined with Mucinous Materials Derived from the Hog Stomach. *George B. Jerzy Glass and Linn J. Boyd,** Department of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals, New York.

In view of earlier observations of the authors

concerning the relationship of glandular mucoprotein of human stomach to Castle's intrinsic factor, 20 patients with pernicious anemia in relapse were treated under rigidly controlled conditions with small oral doses of vitamin B₁₂ in combination with intrinsic factor-containing mucinous materials processed by various methods from the hog stomach. The following animal sources of intrinsic factor were used: (a) acetic acid extracts of hog pyloric mucosa; (b) mucinous materials precipitated by acetone or saturation with ammonium sulfate from hydrochloric acid extracts of hog pyloric mucosa; (c) mucous fractions obtained by further fractionation of above extracts in the Kirkwood electroconvection apparatus; (d) intrinsic factor concentrate of hog stomach combined with small doses of vitamin B₁₂.

Results obtained indicate the feasibility of attaining clinical and hematologic remission in pernicious anemia when small daily doses (10-15 µg.) of vitamin B₁₂ are given by mouth for from 4 to 6 weeks in combination with 50-100 mg., or less, of mucinous materials processed by various techniques from the hog stomach.

One of the oral preparations studied gave strikingly uniform results, characterized by an impressive clinical remission including marked improvement of neurologic disturbances, suboptimal and protracted rise in reticulocytes, and an optimal and sharp increase in erythrocytes, hemoglobin and hematocrit values roughly comparable to that obtained with 1 standard USP unit of antianemia preparations.

Maximal and most rapid results were obtained when a single oral dose of 150 µg. of vitamin B₁₂ was given by mouth in combination with 250-500 mg. of intrinsic factor concentrate from the hog stomach once a week, without any other treatment in the interval. Hematopoietic and clinical responses obtained in these instances were roughly equivalent to those achieved with weekly intramuscular administration of 15-30 µg. vitamin B₁₂ or 10 USP units of liver injection.

Studies on the Use of Citrovorum Factor in Megaloblastic Anemias. *R. Janet Watson, Herbert C. Lichtman, Jacqueline Messite,* Harold Conrad, Jr.,* Rose Ruth Ellison and Victor Ginsberg,* Department of Medicine, College of Medicine, State University of New York at New York City, Brooklyn.

The interrelationships of Citrovorum factor (C.F.) to vitamin B₁₂ in the therapy of anemias are still obscure. Six patients with megaloblastic anemia treated with C.F. illustrate some of the problems involved. One patient with addisonian pernicious anemia had a complete hematologic remission induced by C.F., but after four months of maintenance therapy, developed acute combined system disease, which was quickly reversed by change of therapy to vitamin B₁₂ given parenterally. Another patient with addisonian pernicious anemia had a good remis-

sion induced by vitamin B₁₂. Her failure to continue treatment, and a grossly inadequate diet, resulted two years later in a megaloblastic relapse, which did not respond to vitamin B₁₂. Administration of C.F. produced a remission. A possible interpretation is that she had developed a complicating nutritional deficiency of C.F.

Four other patients had nutritional megaloblastic anemia with remissions induced by C.F., 2 of them, after failure to respond to parenteral vitamin B₁₂ in an initial 10-day period. One patient, a chronic alcoholic on a very poor diet, had an excellent remission induced by vitamin B₁₂. His anemia relapsed two years later despite continuation of adequate vitamin B₁₂ therapy. The administration of C.F. then produced a remission. It is thought that he responded to B₁₂ initially because he was not completely depleted in C.F. When depletion became complete, he required C.F. therapy.

Observations on the Mechanism of Splenic Anemia.

Clement A. Finch, Vikul Viranuwatti and Daniel H. Coleman,** Department of Medicine, University of Washington, School of Medicine, Seattle.

Erythrocyte destruction rate has been correlated with the studies on spleens removed at operation in patients with splenomegaly and anemia. Rates of cell destruction were determined by radioiron, urobilinogen and Ashby techniques. Splenic studies included total splenic red cell mass, in vivo mixing curves employing tagged cells, osmotic fragility, cell volume, and reticulocyte determinations on peripheral, sinusoidal and pulp blood.

Erythrocytes contained within the spleen amounted to as much as 650 ml. or up to 40% of the total red cell mass. Splenic red cell sequestration could be detected by the disparity between T1824 and P₃₂ blood volume determinations, when the splenic red cell mass constituted more than 15% of the total erythrocyte volume.

Variations in the distribution of erythrocytes between the pulp and sinusoids of the spleen and abnormalities in pulp erythrocytes will be discussed.

It is concluded that (1) the spleen may increase hematopoietic demands by holding a large number of erythrocytes, and (2) that the spleen exerts a variable hemolytic effect.

The mechanism of splenic destruction is thought to be dependent on either an abnormal erythrocyte which is selectively taken up and destroyed in the spleen, or an enlarged pulp compartment capable of destroying normal erythrocytes.

The Auto-Immune Hemolytic Anemia of Malignant Lymphocytic Disease. *M. C. Rosenthal, A. V. Pisciatto,* H. Goldenberg, and W. Dameshek,** Blood Research Laboratory, New England Center Hospital, and the Department of Medicine, Tufts College Medical School, Boston.

Abnormal hemolysis as a cause for anemia in

malignant diseases involving the lymphoid system is gaining increasing recognition. Although many cases presenting such anemia lack the usual accompaniments of hemolysis ("occult" hemolytic anemia), others present numerous features of frank hemolysis ("overt" hemolytic anemia). Nevertheless, case detection in the latter group is almost as poor as one might expect of the former.

In an effort to delineate the clinical and laboratory picture of such a syndrome, 20 cases of frank hemolytic anemia, 4 associated with lymphosarcoma, and 16 with chronic lymphocytic leukemia, were studied. Among the latter group, 8 were well documented cases of apparently uncomplicated chronic leukemia, known for one-half to five years. The other 8 were diagnosed only when symptoms referable to hemolytic anemia necessitated medical aid. In contrast, only one case of lymphosarcoma was diagnosed prior to the discovery of hemolytic anemia. The remaining 3 cases were detected after hemolytic anemia had been present for weeks to months.

The physical examination in all cases represented a combination of the findings associated with hemolytic anemia and lymphocytic disease. This often led to splenomegaly of unusual degree and disproportionate to the size of the lymphadenopathy. The laboratory findings paralleled the above, there being anemia, reticulocytosis, spherocytosis, and bilirubinemia of the indirect type, as well as elevated white cell counts in the cases of leukemia. The bone marrow often showed a diagnostic "duality of proliferation," hyperplasia of erythroid and lymphoid elements existing side by side.

Immunologic studies indicated that the mechanism of hemolysis in these cases differed in no respect from that seen in "idiopathic" autoimmune hemolytic anemia. The direct Coombs test was positive in all 16 cases in which it was employed. Circulating panagglutinins were demonstrated in 10 of 15 cases so tested. Routine screening of patients with malignant lymphocytic disease by the Coombs test resulted in the detection of a potential hemolytic mechanism in 2 patients at a time when no anemia was present. Subsequently, both patients developed frank hemolytic anemia.

Reliance on the traditional x-ray therapy or even the newer chemotherapeutic agents for suppression of the hemolytic complications in lymphosarcoma and chronic lymphocytic leukemia is misplaced, since in some cases, therapy by these means seemed to precipitate the hemolytic episode. At the present time, control of hemolysis must be established independently of control of lymphocytic proliferation. ACTH and related hormones, transfusions and in selected cases splenectomy make management of this complication easier.

The Nature of Serum Enhancement of the Canine Isohemagglutinin A: Role of Conglutinin. Frederick

Stohlman, Jr., Hematology Laboratory and the Department of Medicine, Georgetown University School of Medicine, and Georgetown University Hospital Washington, D. C.

The canine erythrocyte isoantibody A, initially described by Young, is a unique isohemagglutinin in that it requires a heat-labile component of serum for the manifestation of maximum agglutinative capacity. Complement fixation by antigen-antibody precipitates removes the enhancing effect of fresh canine serum. However, guinea pig serum fails to restore this activity. The present study was initiated in an effort to clarify this mechanism.

Inactivation of the components of complement (C), C'1, 2 by heat at 56° for 30 minutes, C'3 by zymosan, and C'4 by NH₃, and separation of fresh serum into pseudoglobulin (containing C'2, 4), and euglobulin, (C'1, 3), fractions resulted in a loss of this potentiation of anti-A by fresh serum. Moreover, the concentration of Mg⁺⁺, a cation essential for complement reactions, influenced the canine A reaction. Binding of Mg⁺⁺ inactivated the serum factor and in a significant excess Mg⁺⁺ reduced its activity.

In the presence of fresh absorbed bovine serum, canine anti-A produced agglutination equivalent to that observed in fresh homologous serum. Inactivation of bovine complement destroyed this effect. A cells sensitized with a suitably diluted inactivated anti-A serum fail to agglutinate in the presence of fresh autologous serum diluted 1:10 with buffered saline. If inactivated bovine serum diluted 1:10 is added to a similar system, 4+ agglutination resulted.

These data, together with the demonstration by the antiglobulin technic that sensitization occurs in the absence of complement, suggest that the enhancement of the canine isohemagglutinin A by fresh serum is a conglutination reaction. In conglutination, as described by Bordet and Streng, sensitization of cells without agglutination occurs in the absence of complement. However, complement and conglutinin, a protein-rich in bovine serum, are required for clumping to occur.

Observations on the Wide Spectrum of in Vitro and in Vivo Behavior of Immune Isoantibodies in Dogs. William A. O'Brien, Jr., S. N. Swisher, Jr. and L. E. Young, University of Rochester School of Medicine and Dentistry, Rochester.

Immune isoantibodies of eight specificities have been identified in the sera of transfused dogs. Each isoantibody has been investigated with regard to the following characteristics: thermal amplitude, heat stability, capacity to fix complement and to sensitize erythrocytes for phagocytosis by monocytes or granulocytes, effect of pH and various serum components on agglutinin and hemolysis titer, ability to agglutinate trypsinized red cells, to exhibit the blocking phenomenon and to render erythrocytes agglutinable by antiglobulin serum.

Plasma-containing isoantibody was transfused

into suitable recipient dogs in 32 experiments designed to explain the mechanisms of red cell destruction in the presence of antibody. Detailed serologic and hematologic observations were made during and after these transfusions and in some instances changes in pigment excretion were also measured. Results of these experiments, like those obtained by transfusing red cells into immunized recipients, show that dog isoantibodies vary considerably in their ability to accelerate destruction of erythrocytes *in vivo*. Transfusion of sufficient incompatible plasma may produce morphologic and serologic changes lasting as long as two months. Only those antibodies capable of hemolyzing red cells *in vitro* in the presence of complement-produced hemoglobinemia *in vivo*. Slower destruction of erythrocytes *in vivo* by "nonlytic" isoantibodies is probably effected by a number of mechanisms.

Changes observed during these experiments resemble in many respects those seen in patients with acquired hemolytic anemia and in recipients of blood from dangerous universal donors. Erythrocyte-isoantibody systems in dogs provide a promising experimental approach to the study of the mechanisms of red cell destruction.

Biologic Test for the Demonstration of Erythrocyte-Bound Antibody in Acquired Hemolytic Disorders.

*Gerald Miller** (introduced by *L. E. Young*), University of Rochester School of Medicine and Dentistry, Rochester.

Recent renewed interest in the role of antibodies in hemolytic disorders prompted an investigation of the usefulness of anaphylaxis in the guinea pig as a technic for demonstrating erythrocyte-bound antibody.

In control experiments, the intraperitoneal injection of thoroughly washed red cells from normal persons rarely sensitized guinea pigs for severe shock when challenged by intravenous injection of purified human gamma globulin. This suggests that there is little in common in the antigenic structure of erythrocytes and gamma globulin. Washed red cells from 5 cases of "auto-immune" acquired hemolytic disease with strongly positive direct antiglobulin tests uniformly sensitized guinea pigs for severe (usually fatal) anaphylactic shock upon subsequent challenge with human gamma globulin. Cells were obtained from 4 of the patients during periods of relative remission and from one case in a phase of accelerated hemolysis. Cells from 2 cases of inactive acquired hemolytic disease obtained when the direct antiglobulin test was very weak and a third in which the antiglobulin test has become negative failed to sensitize pigs to gamma globulin. Cells from 2 infants with erythroblastosis due to Rh incompatibility induced anaphylactic sensitivity to gamma globulin, but cells from 2 infants with hemolytic disease due to A-O incompatibility did not.

The results indicate that antigenic analyses

based on anaphylaxis may be useful in investigation of hematologic disorders and may prove applicable to the study of problems which present difficulties in the utilization of agglutination tests or precipitin tests.

Differentiation of Serum Proteolytic Enzymes. N.

Raphael Shulman, Naval Medical Research Institute, National Naval Medical Center, Bethesda.

Serum proteolytic activity has been held responsible for a variety of physiologic phenomena. The proteolytic activity which occurs when serum of various species is treated with chloroform or streptokinase and that which occurs spontaneously in humans in certain pathologic conditions has been considered due to a single enzyme called "plasmin" or "fibrinolysin." In the present study, differences between these enzymes were demonstrated.

Various reactions of human-chloroform-enzyme (HCE), human-streptokinase-enzyme (HSE), the natural protease present *in vivo* in patients following typhoid vaccine (NP), and bovine-chloroform-enzyme (BCE) were compared. Fibrin and fibrinogen tagged with I^{131} , hemoglobin, casein, and prothrombin were used as substrates. HCE digests fibrin but not fibrinogen, has two distinct pH optima with fibrin, at 7.1 and 7.8, is only slightly inhibited by serum antiprotease, and does not digest prothrombin. HSE digests fibrin faster than fibrinogen, has a single pH optimum at 7.1, is markedly inhibited by serum antiprotease, and has been reported to digest prothrombin. BCE digests fibrinogen faster than fibrin, has a single pH optimum at 7.8, is moderately inhibited by serum antiprotease, and has also been reported to digest prothrombin. NP is similar to HCE in its reactions.

Differences in reaction have been demonstrated for at least three distinguishable enzymes formerly assumed to be identical in reaction. Other differences were observed, but those presented are most helpful in understanding the physiologic significance of serum proteolytic activity which will be discussed.

Differences between the Activity of Mature Granulocytes in Leukemic and Normal Blood. A. I.

*Braude, Joyce Feltes** and *Martin Brooks**, University of Michigan Hospital, Ann Arbor.

Phagocytic activity of leukocytes in 45 cases of leukemia was studied by 2 methods: (1) Suspensions of leukemic and suspensions of normal leukocytes, containing approximately equal numbers of mature granulocytes, were inoculated with opsonized Type 2 pneumococcus and phagocytosis by leukemic compared with normal granulocytes. (2) Heparinized leukemic blood was divided into 2 portions and buffy coat removed from one to lower the leukocyte count to approximately 10,000. Each portion was inoculated with pathogenic staphylococci and the number of culturable staphylococci was counted after 6 hours incubation.

Pneumococci were phagocytosed by fewer mature granulocytes from chronic granulocytic leukemia than by normal granulocytes. In lymphocytic leukemia, phagocytosis of pneumococci by granulocytes was usually normal. Treatment of 3 patients with P_{32} restored normal phagocytosis in granulocytic leukemia. Similarly, in granulocytic leukemia, blood with counts of 5,000 to 10,000 mature granulocytes frequently could not lower significantly the number of culturable staphylococci. Yet normal bloods averaging 4,000 mature granulocytes markedly reduced numbers of staphylococci. If buffy coat was not removed, blood from chronic granulocytic leukemia also reduced markedly the number of staphylococci. In lymphocytic leukemia, blood containing less than 2500 mature granulocytes frequently reduced the number of staphylococci.

In chronic granulocytic leukemia, phagocytosis by individual granulocytes is usually impaired but overproduction of granulocytes raises the total defense of the blood to normal. In chronic lymphocytic, and certain acute leukemias, individual function of the granulocytes is usually undisturbed but reduced numbers lower antibacterial defense.

Production of Nucleophagocytosis and the "L.E." Phenomenon by Rabbit Antileukocytic Serum.
Hyman J. Zimmerman, John R. Walsh and Paul Heller, Department of Medicine, Veterans Administration Hospital, Omaha.

The factor responsible for the "L.E." phenomenon in patients with systemic lupus erythematosus has been found to be associated with the gamma globulin fraction of the plasma. It has been suggested that this phenomenon represents an immunologic mechanism. The supposition that the "L.E." factor might be an antileukocytic antibody led the authors to study the effects of an antileukocytic serum on leukocytes in vitro.

Sensitizing material consisted of leukocytes which were dried, thoroughly ground and suspended in isotonic saline. The source of these leukocytes included the buffy coat layer from the blood of patients with granulocytic leukemia in some of the experiments and the buffy coat layer of bovine blood in others. Suspensions of the dried leukocytes were injected subcutaneously into rabbits at 3-day intervals. Plasma obtained from the rabbits was then studied for its ability to reproduce the "L.E." phenomenon when mixed with leukocytes from the source used for sensitization.

All elements of the "L.E." phenomenon, the "L.E." cell, rosettes and the "pre-L.E." cell, were produced by mixing antileukocytic serum with leukocytes from the same source as the antigen. Prior to sensitization, plasma from the rabbits failed to induce the phenomenon. The ability of the rabbit plasma to induce the "L.E." phenomenon seems therefore a result of sensitization to leukocytes. The

similarity of the "L.E." cells and the associated changes produced by antileukocytic serum to the naturally occurring "L.E." phenomenon suggest that the latter may also be due to an antileukocytic antibody.

"Acute" versus "Chronic" Idiopathic Thrombocytopenic Purpura (ITP).
Mario Stefanini, William Dameshek and Peter Bernfeld,* New England Center Hospital and Tufts College Medical School, Boston.*

Greatly variable onset, course, outcome of ITP have been emphasized, especially with regard to differentiation of "acute" and "chronic" forms. Of 75 cases of ITP observed in the past 4 years, 20 "acute" and 20 "chronic" consecutive cases were studied in detail: (a) "Survival time" of injected platelets was <12 hours in "acute," and 12-36 hours in "chronic" cases. (b) Platelet agglutinins were searched for by incubating, in Siliconized glassware, fresh normal plasma rich in Group IV(0) platelets ($\frac{3}{8}$ volume) with the same platelet-free plasma ($\frac{3}{8}$) and patient's platelet-free plasma ($\frac{3}{8}$). Agglutinins were found in 9 of 20 "chronic" patients, and the plasma of 11 induced significant thrombocytopenia when injected into normals. Plasma of only one "acute" case agglutinated normal platelets, but failed to induce thrombocytopenia in vivo. (c) Plasma electrophoresis disclosed a characteristic anomaly (disappearance of α_2 and α_3 peaks and presence of fast α -component α_2) in 18 "acute" and only 2 "chronic" cases. The same abnormality has been found in all 14 cases of hemophilia and 6 cases of Henoch-Schönlein purpura studied (Proc. Soc. Exper. Biol. & Med. 77: 551, 1951). The impact of these findings on pathogenetic interpretation of the disease will be discussed.

"Acute" and "chronic" cases were thus clearly differentiated. Eleven of the "acute" cases recovered spontaneously within 4 months; 6 recovered following splenectomy within 3 months of onset; 3 failed to respond to splenectomy, 2 dying and one recovering spontaneously later. Except in the occasional case in which there is bleeding uncontrolled by ACTH and platelet transfusions, splenectomy should not be performed in "acute" idiopathic thrombocytopenic purpura.

The Site of Action of the Thrombopenic Factor in Human Blood.
Howard R. Bierman, Keith H. Kelly, Laurens P. White, Fauno L. Cordes,* Ralph L. Byron* and Aline M. Littman,* Laboratory of Experimental Oncology, National Cancer Institute, National Institutes of Health, Public Health Service, Federal Security Agency and the Department of Medicine, University of California, School of Medicine, San Francisco.*

Plasma obtained from patients with idiopathic thrombopenic purpura has been shown by Harring-

ton et al. to possess the ability to reduce the circulating platelet level in normal man for periods up to 4 days. Transient falls in platelet count have been observed following the transfusion of fresh whole blood from normal or leukemic donors.

Clinical observations revealed that on 42 instances in 30 patients in whom bleeding started or continued after transfusion of whole bank blood, the mean platelet counts in the patients were below 100,000 per cu. mm. The transfusion of red cell mass was accompanied by bleeding on only 2 of 30 similar occasions.

Frequent simultaneous blood samples were taken from the pulmonary conus or hepatic vein and the femoral artery or vein for 2 to 10 days on 12 occasions in 11 patients during the transfusion of plasma or whole blood, from 4 patients with idiopathic thrombocytopenic purpura, 2 patients with leukemia and one normal donor. In one instance, a saline extract of the spleen of a patient with idiopathic thrombopenic purpura was given to the same recipient who previously had received a transfusion of whole blood from the same patient. In most instances the venous platelet count fell 1 to 8 hours before the arterial platelet count. Thereafter, the arterial platelet count decreased gradually to the venous level.

The data suggest that human plasma causes prompt withdrawal of platelets from the circulation of human recipients. There is no evidence that the responsible substance is the same as that in patients with various thrombocytopenic states. The site of action of the thrombopenic substances appears to be the capillaries. No single organ is primarily involved. The pulmonary circulation is capable of maintaining the peripheral arterial platelet count for up to 8 hours without venous return of these blood elements.

Antihemophilic Activity of Beef Plasma in Vitro.

Theodore H. Spaet, Department of Medicine, Stanford University School of Medicine, San Francisco.

The antihemophilic activity of various agents was measured on the basis of their ability to produce in vitro prothrombin consumption in blood of standardized, severe hemophiliacs. Human plasma suffers a profound loss of antihemophilic activity following short periods of storage, and derived protein fractions have been found to contain a poor yield of active material. Various anticoagulants did not retard the deterioration of antihemophilic activity.

The antihemophilic activity of fresh beef plasma was found to be several times as potent as that of fresh human plasma. This activity is quite stable, no appreciable loss occurring with storage. Two beef fractions were prepared: one by the "acid globulin" technic, the other representing Cohn's Fraction I. In both cases the fibrinogen was pre-

cipitated by heating to 56°C. Upon reconstitution to the original volume of plasma from which the fractions were derived, each was found to have at least twice the antihemophilic activity of fresh human plasma. Their protein content was less than 10% of that in the original plasma, and consisted mainly of beta globulins on electrophoretic analysis. Sheep and hog plasma also showed stable antihemophilic activity, and likewise yielded potent fractions.

Studies are in progress to test the antigenic properties and toxicity of these animal antihemophilic fractions in the hope that an effective agent may be developed for the treatment of hemophilia.

Prophylactic Thromboembolic Control with a New Hypoprothrombinemic Agent. *John B. Field, Martin S. Goldfarb,* Arnold G. Ware* and George C. Griffith,** Department of Medicine, School of Medicine, University of Southern California and the Los Angeles County General Hospital, Los Angeles.

An indandione derivative (diphenyl-1,3-indandione) (Dipaxin) produced a marked hypoprothrombinemia in rabbits. Given orally to humans in single doses of 10-30 mg., it resulted in a strong hypoprothrombinemia persisting 6-10 days. A dose of 4 mg. provided a detectable hypoprothrombinemia and its effects were predictable and reproducible. Hypoprothrombinemia induced with this agent was readily reversible with vitamin K.

About 75 patients with thromboembolic disease, most of which were acute myocardial infarctions, received satisfactory anticoagulant control with this agent. In addition, 7 patients discharged from the hospital with a prognosis suggesting the possibility of recurrent thrombosis or embolism have been maintained on anticoagulant therapy in the ambulatory state. These have received daily medication ranging from 2 to 10 mg. over periods of from 1 to 6 months. Levels of hypoprothrombinemia within the range considered therapeutically desirable have been maintained with relative ease. Control prothrombin determinations have been required only once weekly or once every two weeks. There has been no bleeding complication and no toxic phenomena of any type have been observed. There has been no thromboembolism in the treated patients.

Anticoagulant and Serum Lipid Studies with a New Synthetic Heparinoid. *John B. Field, George D. Ramsay* and Paul Starr,* Department of Medicine, School of Medicine, University of Southern California and the Los Angeles County General Hospital, Los Angeles.

A new pectic acid derivative, Treburon, has been studied both as an anticoagulant and, in comparison with heparin, as a factor altering the physical state of serum lipids. Following a fat meal, both heparin and Treburon were equally effective in producing a sharp fall in the lipomicroemia as meas-

ured in the dark-field microscope. Although both anticoagulants reduced the Svedberg flotation fractions, heparin appeared to be more effective in reducing the Sf 12-35 particles. However, when given repeatedly, Treburon significantly suppressed both the chylomicron count and all the Svedberg fractions of the fasting serum, whereas heparin was relatively ineffective.

In control studies, Treburon compared favorably with heparin as an anticoagulant. Uniform hypocoagulability was obtained even in patients with renal and liver disease. Treburon was given intramuscularly with excellent therapeutic hypocoagulability to 81 patients with thromboembolic disease, 55 of whom had acute myocardial infarction. The drug was given as the sole anticoagulant to about half the patients and daily for periods up to 5 weeks. A high incidence of alopecia (up to 80%) and diarrhea (up to 30%) was seen as an unexpected and uncontrollable effect. This was delayed in some instances for as long as 4-6 weeks after the drug was discontinued. These observations have made further clinical use of this agent untenable.

The Clinical Study of a New Oral Anticoagulant, Dipaxin (2-diphenylacetyl-1,3-indandione). *Luke R. Pascale, and John H. Olwin,** Departments of Medicine and Surgery, Presbyterian Hospital, affiliated with the College of Medicine, University of Illinois, and the Hektoen Institute for Medical Research of the Cook County Hospital, Chicago.

Dipaxin (2-diphenylacetyl-1,3-indandione) has been found experimentally to be an active hypoprothrombinemic agent, having 200 times the potency of Dicumarol and 1,000 times the potency of Tromexan. In the experimental animal Dipaxin acts as rapidly as Tromexan and has the sustained effect of Dicumarol.

In order to evaluate its prothrombinopenic effect in humans and to determine efficient methods of controlling this effect, Dipaxin has been administered orally to 75 patients. Prothrombin levels were measured in all blood samples by both the one-stage and the two-stage methods. Thirty patients were given single doses, starting with 1 mg. in the first patient and increasing to 25 mg. Prothrombin levels were observed for from 5 to 18 days after administration. The remaining patients were given Dipaxin in an effort to induce and maintain therapeutic hypoprothrombinemic levels. The longest period of Dipaxin administration was nine weeks. In each of 7 patients, Dipaxin, Tromexan and Dicumarol were administered to compare their respective prothrombinopenic effects. The effect of various active vitamin K preparations on Dipaxin-induced hypoprothrombinemia was observed.

The results of this study will be reported, and a comparison of the hypoprothrombinemic effect of

Dipaxin with that of other anticoagulants will be discussed.

Paper Electrophoresis of Abnormal Hemoglobins.

*Milton Paul and Arno G. Motulsky,** The Departments of Cardio-respiratory Diseases and Hematology, Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington, D. C.

Paper electrophoresis of 3% non-dialyzed oxy-hemoglobin solutions (0.005 cc.) on Whatman 3 mm. filter paper strips in Veronal buffer, pH 8.6, ionic strength 0.05 (280 volts for 4 hours) indicates that sickle cell (S) hemoglobin has less anodic mobility than normal adult (A) hemoglobin. A third abnormal hemoglobin (hemoglobin C) moves still less rapidly than sickle cell hemoglobin.

Hemoglobin mixtures were obtained from patients with sickle cell trait, hemoglobin C-trait and hemoglobin C-sickle cell disease, or were artificially prepared from normal and sickle cell anemia hemoglobin. Separation of hemoglobin components into distinct spots can be effected. For practical purposes rough quantitation is possible by visual inspection and comparison of the density of the hemoglobin spots with artificial mixtures of known concentration. Exact quantitative analysis of hemoglobin mixtures may be obtained by cutting between the spots and staining the protein moiety with bromphenol blue which can be measured colorimetrically after elution. Fetal (F) hemoglobin cannot be separated from adult normal hemoglobin under these conditions. In conjunction with the method of alkaline denaturation for the detection of fetal hemoglobin, this technique offers a simple tool for clinical, genetic and anthropologic hemoglobin studies.

Preliminary Studies on the Intravenous Administration of Trypsin. *Paul Rueggesser,* Felix Wroblewski and John S. LaDue,* Memorial Center for Cancer and Allied Diseases, New York.

Trypsin was given in dosages of 1 mg. per Kg. and 250 cc. of normal saline at the rate of 30 to 60 drops a minute to 8 control patients. All patients tolerated such administration without any observable toxic effects, other than local irritation with soreness at the site of the infusion. Local thrombophlebitis with palpable intravascular clots was noted on three occasions. Similar dosages were given to 5 patients with thrombophlebitis and phlebothrombosis without any demonstrable beneficial effect. Trypsin failed to prevent or improve thrombophlebitis consequent to local cut-downs done for the purpose of administering this substance.

Thrombophlebitis developed in the sites of infusion in one patient with polycythemia vera. Vascular clotting was noted in the areas where the infusions were started, even in doses as small as 1 mg./Kg. and always with higher doses. No significant

change was noted in necrotic ulcers in 3 patients with carcinoma of the breast.

A discussion will be given of the results of Trypsin administration in 2 patients who have proven thrombosis of the abdominal aorta.

No change in the complete blood count, urinalysis, sedimentation rate, clotting time, bleeding time, prothrombin time, blood urea nitrogen, bilirubin, cephalin flocculation, thymol turbidity, total protein, A-G ratio, alkaline phosphatase, Mazzini reaction, Coombs test and blood typing were seen following the administration of intravenous Trypsin.

Comparative Effects of Dicumarol and Heparin on Experimental Intravascular Coagulation. *Stanford Wessler*, Yamins Research Laboratory, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School, Boston.

A method was developed for the study of clot formation in isolated venous segments in the dog. Coagulation occurred far more slowly in blood in contact with these endothelial-lined surfaces than in coated vessels currently employed in various in vitro techniques. Studies of several phases of the co-

agulation sequence have demonstrated that a fibrin clot developed prior to the disappearance of demonstrable amounts of prothrombin or the elaboration of measurable quantities of clot accelerators.

Since drug-induced hypoprothrombinemia is currently employed to inhibit intravascular coagulation in man, the effects of Dicumarol and heparin on fibrin deposition were examined in 43 dogs. Severe Dicumarol-induced hypoprothrombinemia and serum prothrombin conversion accelerator (SPCA) deficiency did not demonstrably retard fibrin deposition in an isolated vein segment unless sufficient Dicumarol was administered to prolong greatly the in vitro clotting time. In striking contrast, heparin in therapeutic doses significantly retarded clotting in similarly prepared segments. In animals in which both anticoagulants were given, there was no evidence that the concomitant hypoprothrombinemia had potentiated the clot-retarding effect of heparin. Although it has been previously established that Dicumarol does retard intravascular coagulation, it is clear that, under the conditions of these experiments, the anticoagulant effect of heparin is superior to that of Dicumarol.

CARDIOVASCULAR SYSTEM

Heart • Heart Failure • Circulatory Dynamics Pharmacologic Agents

A Comparison of the Effects of Cortisone, ACTH and Aspirin on Rheumatic Carditis. *Bertrand L. Stolzer, Harold B. Houser and Ernest J. Clark,** Streptococcal Disease Laboratory and the Medical Service, USAF Hospital, Warren Air Force Base, Wyoming, and the Department of Preventive Medicine, School of Medicine, Western Reserve University, Cleveland. (This investigation was conducted under the sponsorship of the Commission on Acute Respiratory Diseases and the Commission on Streptococcal Diseases, Armed Forces Epidemiological Board, and was supported by the Offices of the Surgeons General, Departments of the Army and Air Force, Washington, D. C.)

The comparative effects of ACTH, cortisone and aspirin on the course of rheumatic fever have been studied in a series of 152 young adult airmen hospitalized at Francis E. Warren Air Force Base, Wyoming. This study was done as part of the Co-operative Rheumatic Fever Study under the auspices of the American Council on Rheumatic Fever. The effect of these three drugs on carditis was determined during the first 9 weeks of observation and six and twelve months later.

Treatment was given for a 6-week period to all

patients. Carditis was judged to be present before the start of treatment in half of the patients in each treatment group. Abnormal A-V conduction occurred with similar frequency among the 3 groups, but the duration of abnormalities was slightly longer in the aspirin group. At the 6-month follow-up examination of all patients, those receiving cortisone had the fewest significant systolic murmurs. However, a 12-month follow-up on half the patients showed little difference in the incidence of significant systolic murmurs among the 3 groups. No definite conclusions can be made regarding the superiority of any drug employed in preventing permanent heart damage.

The Incidence and Clinical Manifestations of Cardiac Metastases. *Harry F. Bisel,* Felix Wroblewski and John S. LaDue*, Memorial Center for Cancer and Allied Diseases, New York.

In a review of 500 consecutive autopsies at the Memorial Center for Cancer and Allied Diseases, neoplastic involvement of the heart was found in 106, or 21%, of cases. Since this figure seemed sur-

prisingly high, an analysis was made of individual groups of tumors.

As a group, the leukemias showed the highest incidence of cardiac metastases. In 119 cases, representing 7 types of leukemias, there was leukemic infiltration of the heart in 52 (44%). Next in frequency was the group of malignant lymphomas. There were 74 cases studied, consisting of 6 types, in which there was cardiac invasion in 17 (23%). There were 307 tumors of 61 various types (other than leukemias or lymphomas) in which cardiac metastases were found in 37 cases (12%).

The individual neoplasms are listed with enumeration of total patients studied and the percentage of cardiac involvement. From this study it was learned that malignant melanoma has a higher incidence of cardiac metastases than any other tumor. Although only 3 malignant melanomas were found in this series of 500 autopsies, a secondary investigation was made in which 34 melanomas were studied. In the latter group, cardiac metastases were demonstrable in 15 cases (44%).

From these observations the authors conclude that neoplastic involvement of the heart is much more common than is generally realized. It should be considered as an important etiologic factor in the diagnosis of heart disease. The autopsy findings were correlated with physical examination findings, x-ray configuration of the heart and the electrocardiogram. Physical examination and the teleroentgenogram were considered of little diagnostic value, but the electrocardiographic abnormalities were considered to be significant. These relationships are tabulated and discussed.

Diagnosis of the Eisenmenger Complex by Cardiac Catheterization. *Florence W. Haynes* and Lewis Dexter*, Medical Clinic, Peter Bent Brigham Hospital, and Department of Medicine, Harvard Medical School, Boston.

Diagnosis of Eisenmenger's complex by cardiac catheterization has generally been thought to depend on finding practically identical systolic pressures in the right ventricle, pulmonary artery and brachial artery and some shunt of blood from left to right. In this study, one autopsied case was shown to have equal pressures, a left-to-right shunt and arterial oxygen unsaturation. One other autopsied case showed equal pressures but no shunt in either direction. In this case, systolic pressures rose, but remained equal on exercise. Since cardiac catheterization cannot differentiate the true complex from cor triloculare biatriatum or large ventricular septal defect, these disorders may have been present in 10 other cases with nearly identical pressures with left-to-right shunts. Four other patients have been found to have practically identical systolic pressures without left-to-right shunts, and evidence indicates that such a finding can occur not only in Eisen-

menger's complex but also in patients with high pulmonary vascular resistance of unknown cause (one autopsied case) or in association with mitral stenosis (7 cases), patent ductus arteriosus and possibly atrial septal defect. Their differentiation from the first group in whom the aorta communicates with the right ventricle can best be demonstrated by exercise during which the pressures cease to be identical (2 cases of mitral stenosis). Differentiation of these lesions from each other is exceedingly difficult, however, and it is concluded that cardiac catheterization is of limited value in identifying these various conditions.

The Pulmonary Vascular Resistance in Mitral Valvular Disease. *Murray Rabinowitz* and Lawson McDonald** (introduced by *Lewis Dexter*), Medical Clinic, Peter Bent Brigham Hospital, and the Department of Medicine, Harvard Medical School, Boston.

Cardiac catheterization was performed in 87 patients with mitral valvular disease; 56 subsequently underwent cardiac surgery. Effective mitral valve area was calculated by the hydraulic formula (Gorlin, R., and Gorlin, S. G.: *Am. Heart J.* 1: 51, 1951), cardiac output determined by the direct Fick method, and pulmonary vascular resistance was measured. At operation, actual valve size was estimated by the surgeon. In all, there was good correlation between the findings at catheterization and operation. Cases were divided into three groups. I. Mitral stenosis without significant insufficiency; II. Combined mitral stenosis and insufficiency; III. Mitral insufficiency without significant stenosis.

Pulmonary arteriolar resistance generally was much higher in patients with mitral stenosis than in those with mitral insufficiency. Pulmonary arteriolar resistances of 1000 to 2000 dynes seconds cm.⁻⁵ were common in patients with severe mitral stenosis; they did not occur in severe mitral insufficiency. Intermediate values were found in the combined group. Cardiac index bore an inverse relation to pulmonary arteriolar resistance in all groups; in the presence of mitral insufficiency a lower cardiac index occurred than in cases of mitral stenosis with a similar pulmonary arteriolar resistance. In this study, pulmonary vascular disease appeared most marked in cases with severely narrowed valves and was accompanied by a greatly decreased cardiac index. In patients with significant mitral insufficiency, a low cardiac output was also found, but might occur with a much lower degree of pulmonary vascular disease.

Observations on Pulmonary Wedge Pressure Curves. *Aaron Shaffer* and Earl N. Silber*, Cardiovascular Department, Medical Research Institute, Michael Reese Hospital, Chicago.

Cardiac catheterization of young people with congenital heart disease reveals that so-called pul-

monary venous capillary (PVC) and left auricular (LA) pressure curves may be very similar in contour. Analysis of PVC pressure curves in cases of rheumatic valvular disease demonstrates that contour usually gives little indication of the nature of mitral valve obstruction, although the mean pressure may be considered as a reliable index of the severity of mitral valve obstruction. The basis for the discrepancy between LA pressure curve contour, the type of mitral valve obstruction, and the PVC pressure curve in cases of rheumatic valvular disease is discussed.

The Syndromes of Stenotic, Insufficient, and Mixed Mitral Valvular Disease. *Lawson McDonald** and *Murray Rabinowitz** (introduced by *Lewis Dexter*), Medical Clinic, Peter Bent Brigham Hospital, and Department of Medicine, Harvard Medical School, Boston.

Eighty-seven patients with mitral valvular disease were examined to determine whether stenosis or insufficiency were predominant. Methods of investigation included clinical, electrocardiographic, radiologic examinations, also cardiac catheterization, determination of cardiac output and measurement of pulmonary pressures. Respiratory symptoms occurred in severe mitral stenosis, in mixed valvular disease, and in mitral insufficiency in the presence of left ventricular failure. Severe stenosis caused a right ventricular type of apex beat, and incompetence, left ventricular. A loud first heart sound and opening snap was a reliable indication of mitral stenosis, almost always excluding significant insufficiency. Apical systolic and rumbling diastolic murmurs were the rule in insufficiency and stenosis, respectively; their absence did not exclude these conditions nor did their presence indicate either to exist in a hemodynamically significant degree. Right ventricular hypertrophy on the electrocardiogram indicated predominant mitral stenosis, and left, frequently pure mitral insufficiency; but left, combined, or no ventricular hypertrophy was less indicative than right in determining the predominant lesion. On x-ray, right ventricular enlargement and a prominent pulmonary artery and branches in mitral stenosis contrasted with the left ventricular enlargement, inconspicuous pulmonary artery and clearer lung fields of insufficiency. Increased pulmonary arteriolar resistance and low cardiac output were common in advanced mitral stenosis; comparable pulmonary vascular disease was absent in severe insufficiency. It is concluded that the syndromes of pure mitral stenosis and insufficiency can easily be differentiated and that in mixed mitral valvular disease the predominant lesion can be determined in the great majority of patients.

Syndrome of Mitral Insufficiency following Posterior Infarction. *Richard Gubner*, Medical Research Department, Equitable Life Assurance Society

of the U. S., and Department of Medicine, Kings County Hospital, Brooklyn.

Development of a loud systolic murmur following acute myocardial infarction has been described in association with perforation of the interventricular septum and ruptured papillary muscle. These complications occur secondary to extensive infarction with fatal termination in a short period. In contrast, a group of 6 cases is described with prolonged survival following posterior infarction in whom true mitral insufficiency developed. The clinical picture presented by these patients included: (a) appearance and persistence of a harsh, prolonged, grade 3 to 4 systolic apical murmur, (b) enlargement of left atrium and left ventricle, (c) roentgenographic evidence of mitral insufficiency. In 5 of these 6 cases, marked cardiac enlargement and congestive heart failure developed and persisted following recovery from the acute attack of infarction.

Closure of the mitral valve depends not only on the valvular cusps, but also on the integrity of contraction of the musculature surrounding the mitral ring area. As shown by Roy and Adami in 1894, and more recently by Hurwitz, the circumference of the mitral ring orifice is greatly diminished to half its size in systole by a sphincter-like contraction of the surrounding ventricular musculature. Impaired contraction causes failure of the mitral ring to be narrowed sufficiently to allow effective bridging of the mitral cusps, resulting in incomplete valvular closure and mitral insufficiency. Organic mitral insufficiency, therefore, need not necessarily be due to valvular disease, as has been classically considered, but may result, too, from impaired contraction of the musculature surrounding the mitral ring.

Analysis of Physiologic Measurements on 17 Patients before and after Mitral Commissurotomy.

*Robert L. Grissom, Luke R. Pascale, Louis A. Selverstone and Angelo P. Creticos,** University of Illinois, College of Medicine, Chicago.

Cardiac catheterization was performed before and after commissurotomy on 17 patients, of Group III severity, ranging in age from 26 to 52. None was in failure at either time. Five were in atrial fibrillation at the time of preoperative measurements and there were no additional ones at time of second procedure. Symptomatically, all but one were improved. Pulmonary arterial mean pressure was lessened in 11 of 17 at rest, 11 of 15 with mild exercise. None returned to normal range. Pulmonary arteriolar resistance decreased in 7, did not change in 3, increased in 6. Electrocardiograms have changed somewhat in 10 of the 17, 8 showing lessening of right ventricular hypertrophy and 2 showing an increase. Pulmonary capillary pressure decreased slightly to moderately in 11, rose in 6 at rest. Changes in cardiac output were not significant. Arteriovenous differ-

ences were decreased at rest by greater than 0.5 volume % in 8, unchanged in 6, increased by more than 0.5 volume % in 3. Preoperative calculated mitral valve area ranged from 0.5 to 1.5 sq. cm. and postoperative from 0.7 to 2.9 sq. cm. Comparison of these objective measurements with the symptomatic improvement will be made.

Major Surgery in Patients with Chronic Auricular Fibrillation. *John A. Finkbeiner,* Felix Wroblewski and John S. LaDue*, Memorial Center for Cancer and Allied Diseases, Department of Medicine, New York.

A series of patients with organic heart disease and sustained auricular fibrillation who underwent major surgery of a minimum of one hour's duration has been studied with regard to the predisposing and causative factors in the production of the observed 54 instances of intraoperative cardiovascular complications, the 17 instances of postoperative cardiopulmonary complications, and the 15 deaths from cardiovascular disease. There were 60 patients submitting to 76 operations with a patient-operative mortality of 5%; one of these deaths was due to cardiovascular disease. A recent history of congestive heart failure and inadequate digitalization were the only significant factors in the pre-, intra-, and postoperative periods which could be correlated with an increased cardiopulmonary complication rate.

While the ultimate prognosis of chronic auricular fibrillation depends upon the prognosis of the underlying heart disease and the fortuity in escaping serious complications, the susceptibility of fibrillators to cardiac failure is recognized. The similarity of the changes in cardiopulmonary, renal, and hepatic function during anesthesia and operation and during congestive heart failure are emphasized. Reduction of the operative morbidity and mortality from cardiovascular complications can be accomplished only by careful pre-, intra-, and postoperative evaluation and care. Methods of obtaining this goal are discussed by evaluation of the presented data.

The Hyperactive Carotid Sinus of the Cardiac Inhibitory Type in Auricular Fibrillation. *Jacob Zatz and Louis A. Soloff*, Departments of Medicine, Temple University and Episcopal Hospitals, Philadelphia.

Weakness, dizziness, faintness, syncope and even sudden death in individuals with permanent auricular fibrillation have been attributed to sudden increases in ventricular rate. The occurrence is reported of the hyperactive carotid sinus of the cardiac inhibitory type in 7 of 19 consecutive individuals with permanent auricular fibrillation.

Pressure upon the carotid sinus produced ventricular standstill in 3 of these 7, and abrupt slowing of the ventricular rate in 4. In these 4, the ventricular rate dropped abruptly from 70, 75, 60 and 135 per

minute to 44, 36, 29 and 48 per minute respectively and became regular in rhythm. In each of these, the configuration of the QRS complex changed. The QRS complex became larger in 2, an R was abolished in 1 and in another the configuration of complete left bundle branch block of 9 years' duration was transformed to that of normal conduction. The 3 individuals with ventricular standstill consequent to carotid sinus pressure had recurrent episodes of syncope. One of the others had frequent episodes of dizziness. Symptoms were reproduced by carotid sinus pressure. In the other 12 individuals, carotid sinus pressure resulted in a slight slowing of the ventricular rate without symptoms.

It is concluded that the hyperactive carotid sinus syndrome is at times responsible for transient symptoms of circulatory insufficiency in individuals with auricular fibrillation. The use is discussed of vagal inhibitory drugs to prevent such episodes.

The Comparison of Experimentally Produced Esophageal Pain with Anginal Pain in Patients with Angina Pectoris. *P. Kramer, W. Hollander,* W. Judson and H. Osher,** Evans Memorial, Boston.

Esophageal pain and the pain of angina pectoris are frequently confused clinically. Experimental attempts at elucidation have yielded contradictory conclusions.

This investigation was undertaken to determine the relationship of esophageal pain to the pain of angina pectoris. Thirteen patients with unequivocal angina pectoris and positive exercise tolerance tests (EKG) were studied. Esophageal pain was produced by balloon distention via a Miller-Abbott tube placed fluoroscopically. Simultaneous multi-lead electrocardiographic tracings were taken. Barium swallows were done in each of the patients.

Four of the 13 patients could not distinguish the substernal pain produced by esophageal balloon distention from an attack of angina pectoris. In 1 of these 4 patients on two different tests, the pain also radiated down the left arm. The angina-like pain appeared as the balloon was distended and disappeared immediately with deflation. No ischemic EKG changes were associated in these 4 patients. In a fifth patient, although only minor discomfort was experienced with esophageal distention, electrocardiographic evidence of ischemia appeared.

These findings indicate that esophageal pain is capable of mimicking the pain of angina pectoris and may be indistinguishable. Balloon distention of the esophagus as a clinical aid in differentiating esophageal and anginal pain is of limited value.

Cardiorenal Hemodynamics and Excretion of Sodium and Water, at Rest and during Exercise, in Patients with Mitral Stenosis before and after Mitral Valvuloplasty. *Walter E. Judson, J. D. Hatcher, William Hollander,* Meyer H. Halperin*

and Irwin H. Friedman,* Massachusetts Memorial Hospitals, Boston.

Eight patients with mitral stenosis have been studied with simultaneous measurements of cardio-renal hemodynamics and the excretion of sodium and water, both at rest and during exercise (in the horizontal position), before and after mitral valvuloplasty.

In the group of patients studied there was no consistent correlation between the degree of subjective improvement after operation and the changes in cardio-renal measurements. In none of these patients did the cardiovascular responses to exercise suggest a marked degree of cardiac functional improvement after mitral valvuloplasty.

In 3 patients a moderate improvement in the cardiohemodynamics was observed. However, this improvement was not associated with similar directional changes in renal hemodynamics and excretory functions in every patient. In 3 other patients exhibiting slight improvement in cardiohemodynamics, there were no significant changes in the renal hemodynamics or excretion of sodium and water. In the 2 remaining patients, one of whom had a "sham operation," there were no alterations in either the cardiac or the renal functions measured.

In 2 patients during exercise clinical pulmonary edema with marked elevation of pulmonary "capillary" pressure occurred. This was observed to be associated with a very marked reduction in the glomerular filtration rate with antidiuresis but without a consistent change in the excretion of sodium.

The Work of the Right Ventricle in Patients with Interatrial Septal Defect. *Robert Fraser* and Carleton B. Chapman, Department of Medicine, University of Minnesota, Minneapolis.*

An attempt was made to quantitate the burden placed on the right ventricle by study of 19 adult patients in whom uncomplicated interatrial septal defect was diagnosed by cardiac catheterization. The mean resting pulmonary arterial flow was 17.2 ± 6.2 l./min., and the average mean pulmonary arterial pressure was 21 ± 9 mm. Hg. Use of these values for calculation of RV pressure work gave an average value of 290 Kg.-m./hr. Since ventricular work is expended during systole, use of RV mean systolic pressure yields more accurate, and higher, results (average, 382 Kg.-m./hr.). A simple method for obtaining the RV mean systolic pressure by planimetric integration was used. When the method was applied in the present material, RV pressure work was found to be about 4 times the probable normal value. Although kinetic work could not be calculated in absolute terms, an index to it was obtained by a ratio (pulmonary flow/systemic flow)³, the normal value for which is 1. In 19 cases studied, the value ranged from 8.7 to 143.0, the average being 41.1. Kinetic work, therefore, probably accounts for a considerable portion of total RV work in patients

with IASD. It is concluded that right ventricular pressure work is higher, in cases of IASD, than has been thought, partly because of the use of inappropriate mean pressure values in the calculations. Accurate values for total work cannot be achieved until kinetic energy and that expended as a result of turbulence can be measured.

The Effect of an Arteriovenous Fistula on Red Cell Volume, Plasma Volume and Total Blood Volume. *F. H. Epstein and T. B. Ferguson, Department of Cardiorespiratory Diseases, Army Medical Service Graduate School, Washington, D. C.*

An increase in plasma volume, measured by T-1824, has been shown repeatedly to characterize animals and humans with peripheral arteriovenous fistulas. However, measurements of circulating red blood cell volume, using tagged cells, have not been reported. Seven dogs were studied before and from 2 to 6 weeks after creating an arteriovenous fistula between the aorta and the inferior vena cava. Four animals developed edema or ascites as a result of this procedure. Red cell volume was measured by the dilution of cells labelled with P³², plasma volume by the dilution of T-1824, and total blood volume was calculated by adding the two. In all cases there was an increase in plasma volume (average 30%) and a fall in jugular hematocrit. Red cell volume did not change significantly, although total blood volume increased in every case. In 5 instances there was an increase in the ratio of the jugular hematocrit to "total body hematocrit," after the A-V fistula was created.

The data confirm the previously reported increase in blood volume with an arteriovenous fistula, imply that the total red cell volume need not necessarily be increased, and suggest an altered distribution of plasma and cells in this condition.

Plasma Volume Changes in Congestive Failure.

Melvin A. Goldberg, Robert P. Gilbert and John Rosevear,* Northwestern University Medical School, Chicago.*

Contrary to previously accepted ideas, some recent reports based on labeled red cell methods have shown not only normal red cell volumes but normal plasma volumes in many patients with heart failure. Diuresis was not reported to produce any significant change, although hematocrit figures are incomplete.

In order to clarify this problem we have studied hematocrit and Evans blue plasma volume changes before and after diuresis in 10 patients with congestive failure and peripheral edema. Arterial blood was used to avoid stasis errors, and hematocrits were done in triplicate at 3500 R.P.M. for one hour. In 7 cases there was a clear-cut rise in hematocrit (average 3.1 percentage points). This correlated well with the weight loss but not with venous pressure or circulation time changes. There was poor agreement between plasma volume changes

as calculated from hematocrit differences and as calculated from Evans blue dye results. The average values were fairly close (-430 and -280 ml., respectively).

Assuming no increase in total red cell volume during the period of observation, and assuming no shift of plasma from large to small vessels, it seems clear that there is a drop in plasma volume with recovery from congestive failure.

The Effect of Congestive Heart Failure on the Blood Volume as Determined by Radioactive Chromium-Tagged Red Cells. *Seymour Eisenberg** (introduced by *Donald W. Seldin*), The Medical Service, V. A. Hospital, Dallas, Texas, and the Department of Internal Medicine, Southwestern Medical School of the University of Texas.

The effect of congestive heart failure on the blood volume is a matter of considerable controversy. Measurements with Evans blue dye have yielded results indicating an expanded blood volume during the congestive state, while studies with labeled red cells (P^{32}) have not revealed any consistent changes. The dye method has been criticized because it may be influenced by an expanded lymphatic system, thereby yielding high values, while the P^{32} method suffers from the disadvantage of requiring a short period for equilibration which may be inadequate in the patient with heart failure.

Radiochromium-labeled red cells provide a method which is free from these disadvantages, being sufficiently stable to permit long periods for equilibration and being uninfluenced by lymph flow. A study of the blood volume in patients with various types of heart disease, before and after compensation, has been undertaken, using radiochromium-labeled red cells as the reference substance. Three well defined groups of patients were studied:

(1) Patients in early heart failure with edema, in whom compensation was restored with digitalis alone, were studied before and after compensation. The blood volumes were not increased above the normal for the method; there was no significant change following compensation. (2) Patients with severe and protracted heart failure, requiring mercurial diuretics for compensation, in several instances had increased blood volumes but there was no change following compensation. (3) Compensated cardiacs who were permitted to form edema, studied before, during, and after decompensation. The majority of these subjects exhibited little change.

A Study of Repeatability of Plasma Volume Using I^{131} and T-1824 at Two-Week Intervals. *Harvey Krieger,* Laura Brooks and Scott Inkley** (introduced by *Austin Weisberger*), Cleveland.

The purpose of this study was to evaluate the variation in estimation of repeated plasma volumes done on a group of 13 normal fasting subjects. Plasma volumes were studied by two methods,

I^{131} and Evans blue. After a two-week interval, the studies were repeated, using the same methods. The standard deviations of the distributions of repeated determinations for each of the two methods were estimated to be 156 cc. for Evans blue and 266 cc. for I^{131} . The 95% confidence intervals of the standard deviations are 106 to 288 cc. for Evans blue and 185 to 469 cc. for I^{131} . Although the series is small and the estimates are not statistically significant, it provides some indication of the variability of plasma volume even under controlled conditions.

Tissue Electrolytes in Cardiac Failure. *N. Nichols, A. C. Barger* and G. Nichols, Jr.,* Baker Clinic Research Laboratory, Boston.

The composition of right and left ventricles of dogs in congestive failure was determined and compared with the composition of skeletal muscle in these animals and normal dogs.

Total water content of the ventricles was slightly higher (average: 798 cc./Kg. fat-free tissue) than normal (average: 786). Skeletal muscle water was increased (average: 794) in edematous dogs compared with normals (average: 770).

Concentrations of potassium and phosphate were related to the weight of the intracellular proteins (ICP), defined as dry, fat-free, connective-tissue-free solids. The concentration of potassium in normal skeletal muscle averaged 55 mEq./100 Gm. ICP; phosphorus concentration averaged 33 mM./100 Gm. ICP. In dogs in failure, potassium content was markedly decreased in both skeletal (41) and cardiac muscle, and there was a significantly lower potassium content in the right ventricle (45) than in the left (49). Total phosphate was decreased in skeletal muscle (30), but was increased in right (36) and left (37) ventricles.

The average Na:Cl ratio in an ultrafiltrate of plasma was the same in both normals and dogs in congestive failure (1.24:1). The Na:Cl ratio in normal skeletal muscle was 1.45:1, indicating the presence of intracellular sodium. In tissues of dogs in failure, this ratio was decreased in skeletal muscle (1.14:1) and in both right (1.19:1) and left (1.09:1) ventricles, demonstrating the presence of intracellular chloride in these tissues.

These data indicate that cellular composition is related specifically to tissue activity and will be discussed in relation to the metabolism of skeletal and cardiac muscle in congestive failure.

The Relationship of the Electrocardiogram to the Red Blood Cell Potassium in Diabetic Acidosis. *E. Craige* and H. G. Keitel* (introduced by *Charles H. Burnett*), Department of Medicine and Pediatrics, Massachusetts General Hospital, Boston. (Dr. Craige currently at Department of Medicine, University of North Carolina, Durham.)

The electrocardiogram is known to be affected

by variations in the serum potassium in a variety of conditions. The relationship, however, is often a rough one and the same serum level in different patients may be accompanied by electrocardiographic findings ranging from normal to distinctly abnormal. This has led to speculation that some of the electrocardiographic changes are due to intracellular K changes as well as alterations in the concentration of other electrolytes.

Patients in diabetic acidosis on admission to the hospital often have a high or normal serum K level in the presence of intracellular deficit of this cation. This situation might afford an opportunity to separate the effects on the electrocardiogram of intra- and extra-cellular K changes.

Seven patients with diabetic acidosis were studied during recovery from acidosis. Serial serum chemical determinations and electrocardiograms were made and the intracellular compartment was sampled by RBC analyses, supported in 3 cases by balance studies. It was found that the Q-T interval followed more closely the RBC K concentration than it did the serum K. The height of T waves followed roughly the serum K concentration. The possible influence of pH and concentrations of other electrolytes was considered. Acidosis itself may have been a factor contributing to the persisting elevation of T waves in J. S. in the presence of a very low serum K. This patient was the only one who died. Although initial electrocardiograms in 5 of the 7 cases were distinctly abnormal, all the surviving patients showed a return to normal electrocardiographic patterns.

Cyclic Increases in Cardiac Disability during Menstruation in Women with Rheumatic Heart Disease. *Henry J. Kowalski and Edmund J. Callahan, III,* Boston City Hospital, Boston.*

Premenstrual edema and weight gain noted occasionally in normal women has been attributed to increased retention of salt and water secondary to elevated production of ovarian hormones. Such changes might play a role in the precipitation of increased cardiac disability before menstruation. The present report describes the results of concurrent clinical and laboratory observations on 14 patients with rheumatic heart disease and 9 normal women who were studied early in the menstrual cycle and prior to menstruation.

Seven patients (mean age, 31.6 years) developed increased cardiac disability premenstrually as manifested by increased dyspnea on exertion or at rest, nocturnal dyspnea, increased fatigability, choking sensations and/or palpitation. Signs consisted of right upper quadrant tenderness, basal rales, ventricular premature beats and/or edema. Small but significant increases ($p = .02$) occurred in Evans blue space averaging 10.17%. Three of the 7 patients were classified III; 2, II; and 2, I (Cardiac classi-

fication, New York Heart Association). Five of 7 required digitalis and salt restriction and 4, periodic mercurial diuretics.

Eight patients (mean age, 21.6 years) without premenstrual increases in cardiac disability, and 9 normal women did not increase Evans blue space, nor did their weight change. One of the 8 patients was classified III; 1, II; and 6, I. Only 1 of the 8 required digitalis and salt restriction.

Hematocrit, serum sodium, serum potassium, and total serum protein failed to change in normal women or in patients with heart disease.

Although there is an association between Evans blue space and increased cardiac disability, the space increases may represent altered capillary permeability or shifts of water within the body, since weight gain did not occur. Factors of importance in the premenstrual increases in cardiac disability appear to be cardiac reserve and age of the patient.

Thiamine Excretion in Congestive Heart Failure.

Michael Wohl, Charles R. Shuman, Richard Turner* and John F. Fittipaldi,* Temple University Hospital and Philadelphia General Hospital, Philadelphia.*

The nutritional failure seen in many patients with chronic cardiac decompensation has not been adequately studied in the past. As the first phase of a series of investigations into this problem a group of patients with heart disease in decompensation was examined by laboratory methods for evidence of thiamine deficiency and for the effect of mercurial diuresis upon urinary thiamine excretion. Fifty patients under treatment for heart failure were given loading doses of thiamine using 0.35 mg. per square meter of body surface area (Hochberg and Melnick), following which the 4-hour urinary thiamine content was measured by the thiochrome method. Seventeen control subjects selected from patients with noncardiac disease in good nutritional status or from the hospital personnel were studied by the same method. The mean thiamine excretion of the congestive failure group was 40.6 $\mu\text{g.}$, with a standard deviation of 24.9 $\mu\text{g.}$ The mean excretion of the control group was 139.5 $\mu\text{g.}$, with a standard deviation of 73.5 $\mu\text{g.}$ Statistical analysis of the data indicated that the noncardiac group had a significantly higher excretion of thiamine after a loading dose than the patients with heart disease.

Ten patients with severe heart failure receiving mercurial diuretics in the course of treatment were studied using 24-hour urine collections before, during and after the injection of the mercurial. Five patients were given loading doses of thiamine during the observation period. The 24-hour urinary thiamine content was measured, demonstrating significant increases in thiamine excretion with mercurial diuresis.

Clinical and Investigative Studies Using a New Instrument for the Continuous Recording of Blood Pressure and Heart Rate. *John C. Rose, Saul R. Gilford,* Anton Soler,* Edward A. Parzenope* and Edward D. Freis, Washington, D. C.*

An instrument for the automatic recording of a number of physiologic variables called the "physiologic monitor" has been developed by the National Bureau of Standards. Although it was designed primarily for operating room use in anesthetized patients, a preliminary test program on medical patients indicates that certain of the functions measured, namely blood pressure and heart rate, may be valuable for other clinical or research purposes. Systolic and diastolic blood pressure are recorded accurately quantitatively from a microphone pickup and standard inflatable arm cuff every 3 minutes, while heart rate is recorded every 30 seconds. The apparatus may be left unattended for many hours while a printed record of these physiologic variables is automatically recorded. The apparatus produces little or no discomfort so that patients are able to sleep through the night while the machine is in operation.

The instrument has been found to be particularly valuable in patients with incipient or overt shock due to such conditions as gastrointestinal hemorrhage or myocardial infarction, and in hypertensive patients where the effects of sleep, emotional disturbances and therapeutic procedures, particularly the administration of hypotensive drugs, can be followed with ease and precision. Remote positions of the recorder make it possible to follow changes at a distance, e.g., from the nurses' station or doctors' ward office. Records illustrating these clinical and investigative applications will be presented.

Hemodynamic Changes Induced by Moderate Exercise in the Normal Human Being. *Carleton B. Chapman and Robert Fraser,* Department of Internal Medicine, University of Minnesota, Minneapolis.*

Use of exercise for evaluating cardiovascular function is well recognized, but certain technical barriers have hampered efforts in this direction. Use of a modified dye curve technic for measuring cardiac output was found to overcome some of the difficulties. The modification involves the insertion of venous and arterial catheters and use of heparinized blood instead of serum. Arterial pressure curves were recorded simultaneously. The method was applied to 18 normal men and 11 normal women, both at rest and during treadmill work after a steady state was attained (3 m.p.h. at 5% grade for 10 minutes). The mean resting values for cardiac output (6.93 ± 1.14 L./min. for men and 5.64 ± 1.24 L./min. for women) are comparable to those

obtained with other methods. The mean values during exercise were 10.66 ± 4.49 and 11.62 ± 2.93 L./min., respectively. Percentagewise, the increase was greater for women than for men and there were wide individual variations. The average mean circulation time showed a decrease of $31.7 \pm 12.7\%$ for men and $34.8 \pm 9.7\%$ for women when the exercise stress was applied. At the same time, there was marked decrease in peripheral resistance.

The method is applicable to clinical problems and can be used in evaluating patients with a wide variety of cardiovascular disorders. It is hoped that, among other things, it will eliminate some of the difficulties in quantitative evaluation of patients with asymptomatic heart disease.

Changes in Cardiac Output during the Cold Pressor

Test: Comparison of Low-Frequency Ballistocardiograph and Direct Fick Methods. *Phillipe V. Cardon,* Daniel S. Lukas and Harold G. Wolff.** The Departments of Medicine and Psychiatry, New York Hospital-Cornell Medical Center, New York.

Cardiac output was determined simultaneously by the low-frequency (Nickerson) ballistocardiograph, and the direct Fick method, in 5 normotensive and 3 hypertensive subjects. In each subject measurements were made before, during, and after the cold-pressor test. Initial resting values agreed closely in 3 cases. In one case there was a disparity of 1 L./min., and in 4 cases the disparity was greater than 2 L./min. In 2 hypertensive and 3 normotensive subjects changes in cardiac output of more than 1 L./min. by the Fick method occurred during or after the cold-pressor test. In 3 of these, the pressor response was caused by increased cardiac output and accompanied by a drop in peripheral resistance. In the other 2, the opposite occurred. There was fair relative correlation between the 2 methods in 5 of the 15 possible comparisons. Among the remaining 10 comparisons, 6 types of deviation were noted; namely, changes by BCG in opposite direction when Fick rose or fell; no change in BCG when Fick rose or fell; and rise or fall in BCG with Fick constant. The paired BCG estimates, within each period, in general agreed closely with each other. The 3 subjects who showed no significant changes by the Fick method were those who had the smallest pressor responses. In these subjects the BCG also indicated a steady state.

Hypertension following Bilateral Nephrectomy.

Louis Tobian, Jr., Department of Biological Chemistry, Harvard Medical School, Boston.

Hypertension was found in 53% of rats (29 out of 55) 3 days after bilateral nephrectomy when their diet contained 1% sodium (water ad libitum). This hypertension following bilateral nephrectomy

was found in only 3% (2 out of 61) when sodium was withheld from their otherwise similar diet. Massive doses of DCA during the brief period after bilateral nephrectomy does not produce more hypertension than bilateral nephrectomy alone. In rats on the 1% sodium diet, the hypertension after bilateral nephrectomy can be completely prevented if the adrenals are excised at the time of the nephrectomy (13 rats).

The hypertension in bilaterally nephrectomized rats on a salty diet is not produced just by gains in body water. Half these hypertensive rats gained weight and half lost weight in the 3 days after the second nephrectomy. However, the weight-losing half actually had a slightly higher average blood pressure than the weight-gaining half. Six additional nephrectomized rats on the salty diet gained weight and had no hypertension at all. Moreover, large amounts of Ringer's solution were given to normal rats without producing hypertension. The hypertension is mainly related to the absence of renal tissue and resembles the usual type of renal hypertension in that either a low sodium diet or adrenal insufficiency will largely prevent it. However, here is a type of renal hypertension where a renal pressor substance is obviously impossible, thus weakening the argument for an important renal pressor substance in ordinary chronic renal hypertension.

Experimental Pulmonary Vascular Occlusions, Resulting in Acute Cor Pulmonale, and Simulating "Obstetrical Shock" of Late Pregnancy. *C. L. Schneider, R. M. Engstrom* and A. A. Cintron-Rivera*, Wayne University College of Medicine and Wayne County General Hospital, Eloise, Mich. (Supported in part by the Medical Research and Development Board, Office of the Surgeon General, Department of the Army.)

Acute and widespread occlusion of the pulmonary vascular bed was caused in dogs by intravenous injection of extracts of tissue thromboplastin. This initiates massive and disseminated coagulation within the blood stream, and is believed to result in a kind of submicroscopic "fibrin embolism"; i.e., in formation of fibrillae of fibrin, throughout the circulating blood. As an end result, fibrin builds up microscopically demonstrable, intravascular occlusions of a characteristic structure. These occlusions have a predilection to form in the pulmonary arterial bed. Blood pressures were recorded through catheters in the pulmonary artery and in the aorta. The pulmonary arterial pressure rose to 50 mm. of mercury; the systemic pressure fell to shock levels; the right heart dilated excessively and the left heart filled inadequately. In comparative studies, experimental meconium embolism (in which there is an over-all inhibition, rather than an acceleration, of

coagulation) caused similar, extreme blood pressure changes and acute cor pulmonale. Consistent with the preformed nature of the meconium occlusions, the blood pressure changes were almost instantaneous. By contrast, the pressure changes initiated by "fibrin embolism" required more than one minute to develop, a time lag consistent with the time needed for building up of the fibrin occlusions. Similar fibrin occlusions have been observed postmortem, after maternal abruptio placentae and after eclampsia. It follows that disseminated fibrin occlusion of the pulmonary arterial bed, and resultant acute cor pulmonale, may be a cause of the circulatory failure that is sometimes observed clinically in these acute disorders of late pregnancy.

Circulatory Effects of Aminophyllin in Acute Myocardial Infarction. *Robert P. Gilbert, Melvin A. Goldberg* and Joseph Griffin,** Northwestern University Medical School, Chicago.

Aminophyllin has been widely used in the management of acute myocardial infarction as a coronary dilator and to alleviate cardiac failure. The effects of 0.25 to 0.5 Gm. of aminophyllin given intravenously over a 10-minute period have been studied in 5 patients with acute myocardial infarction. Cardiac output was measured at the bedside by the dye dilution technic, and arterial pressures were recorded with a strain gage manometer. Venous pressure changes were determined with a saline manometer.

In 3 patients with satisfactory repeat output determinations there was no clear-cut change. All three had initial cardiac indices in the normal range. The dye circulation times were shortened in 2 of these patients (36 to 27 and 23 to 16.5 seconds). In the third patient it rose from 18 to 21 seconds. In 4 patients the arterial pressure fell about 10 mm. Hg towards the end of the injection and quickly rose to control levels or higher in 3. The venous pressure fell in each case. There were no significant rate changes. No untoward effects were noted. It may be concluded that when given cautiously, aminophyllin need have no significant depressor effects in acute myocardial infarction. Venous pressures were improved. Further study of its effects in low output with shock is necessary.

The Effect of Intravenous Sodium Amytal on the Cardiorenal Hemodynamics and the Excretion of Electrolytes and Water. *William Hollander,* Walter E. Judson and Irwin H. Friedman,** Massachusetts Memorial Hospitals, Boston.

Cardiac catheterization (Fick) studies were performed in 6 hypertensive patients along with simultaneous measurements of renal (PAH and inulin clearances) hemodynamics and excretion of sodium and water. Sodium amytal was given intravenously in doses of 0.5 to 0.75 Gm. Peripheral mean arterial

pressure fell on the average 20 mm. Hg at the lowest point. Cardiac output, right ventricular and pulmonary arterial pressure did not change significantly. Renal plasma flow, glomerular filtration rate, and (except in one patient) sodium and water excretion also remained unchanged. The data indicate that a decrease in peripheral resistance (including the kidney) and not a reduction in cardiac output is responsible for the hypotensive response to sodium amylal.

Effect of Hexamethonium Bromide on Coronary Flow, Cardiac Work, and Cardiac Efficiency. *C. W. Crumpton, G. G. Rowe,* R. T. Cappa,* G. O'Brien* and Q. R. Murphy,** University Hospital and University of Wisconsin Medical School, Madison.

Cardiac output (Fick method), coronary flow (nitrous oxide technic), and mean arterial blood pressure were determined in 16 normotensive anesthetized dogs before and 30 minutes after 1 mg./Kg. hexamethonium bromide intravenously. MABP fell from 123 to 71 mm. Hg within 1-2 minutes following hexamethonium and stabilized at 107 mm. Hg during the second flow determination. Coronary flow decreased from 106 to 90 cc./100 Gm./min. ($p = .02$). There was a reduction in cardiac work which resulted from a significant decrease in both mean arterial blood pressure (13%) and cardiac output (31%). These changes occurred despite a sinus tachycardia of 142/min. As a result of a greater percentage reduction in cardiac output as compared with blood pressure, the calculated total peripheral resistance was observed to increase. Coronary resistance did not change from control observations. Cardiac oxygen consumption did not change following hexamethonium. This was accomplished by an increase in oxygen extraction from 10.8 to 12.9 vols.%. Coronary sinus oxygen content fell from 5.6 to 2.7 vols.% ($p < .01$). Calculated cardiac efficiency was reduced.

In order to evaluate the effects of changing levels of anesthesia and blood withdrawal, another group of 15 normotensive dogs was studied under identical conditions after administration of 1 cc. physiologic saline solution. Except for a 13% increase in myocardial oxygen extraction at the time of the second flow, there were no significant differences in the mean averages of these two determinations.

Under the experimental conditions described, blood pressure reduction following hexamethonium bromide was the result of a decreased cardiac output.

Clinical Results and Hemodynamic Studies following the Use of Hexamethonium Chloride in the Treatment of Hypertension. *John H. Moyer, Sam I. Miller,* Harvey B. Snyder* and William B.*

*Livesay,** Departments of Medicine and Pharmacology, Baylor University College of Medicine, Houston.

Hexamethonium chloride when administered orally is an effective ganglionic blocking agent for reducing the blood pressure in patients with hypertension. A significant reduction in blood pressure (MBP decreased more than 20 mm. Hg) was observed initially in 86% of 120 patients treated for hypertension on an outpatient basis. The reduction in blood pressure was most marked in the upright position and was returned to approximately normal limits in one-third of the patients treated. Sixty per cent of these patients who were followed for a year or more were adequately regulated with hexamethonium alone. It was necessary to add another drug to the therapy of the remaining patients or discontinue hexamethonium entirely. The amount of hexamethonium required to reduce the pressure was not well correlated with the severity of the hypertension. Patients with combined renal disease and cardiac failure seemed to be the most difficult to control. The greatest problems encountered were the variation in blood pressure from day to day and the constipation. Renal function studies indicated an acute depression following the initial reduction in blood pressure. However, renal hemodynamics returned to control levels despite a maintained reduction in blood pressure. If the reduction in blood pressure was excessive, renal function remained depressed. This is of particular importance in the patient with damaged kidneys. In this instance, only minimal depression of renal function can precipitate frank excretory failure. Therefore, the blood pressure should not be reduced to more than 150 mm. Hg systolic in the upright position. Cerebral blood flow was not altered in the supine position but if the mean blood pressure was reduced below 80 mm. Hg on standing cerebral blood flow decreased. Since the hypotensive response to hexamethonium is predominantly orthostatic, the blood pressure should be regulated in the upright position in order to avoid syncope and other symptoms of cerebral ischemia while standing.

The Effect of Ganglion Blocking Agents in Congestive Heart Failure. *Charles R. Shuman, Norman Learner and John H. Doane, Jr.,** Philadelphia.

Intravenous administration of tetraethyl ammonium (150 to 500 mg.) and hexamethonium (12.5 to 50 mg.) was conducted in a group of 21 patients with congestive heart failure due to hypertensive, arteriosclerotic and valvular heart disease. The effects upon venous pressure, arterial pressure, pulse rate, skin temperature and digit plethysmographic readings, vital capacity and the degrees of dyspnea and orthopnea were recorded. Similar data were obtained in a group of 7 patients

in whom cardiac disease was absent. The venous pressure in the congestive failure patients fell from a mean of 174.5 to 85.0 mm. saline; the mean vital capacity rose from 1620 cc. to 2122 cc. after administration of these agents. The skin temperature and digital plethysmograph readings gave evidence of an increased blood flow in these areas in the nonfailure patients. However, in patients with congestive failure, only 2 of the 11 in whom these data were obtained showed a rise in cutaneous or digital blood flow. Amelioration of the symptoms due to pulmonary congestion, dyspnea and orthopnea, was evidenced to varying degrees in the congestive failure group. Some of these patients were markedly improved. The failure to observe an increase in cutaneous blood flow in the feet and hands in the heart failure patients suggests that the principal action of these drugs was manifested in other areas of increased vascular tone to account for the reduction of venous and arterial pressures. The clinical improvement manifested in this group is probably due to redistribution of the blood volume to regions peripheral to the cardiopulmonary and central venous circuits.

Vascular Responses of the Kidney and Lower Extremity to Six Drugs Used to Lower Arterial Pressure in Man. *Walter Redisch, Lothar Wertheimer,* Claude Delisle* and J. Murray Steele,** Research Service, Third (New York University)

Medical Division, Goldwater Memorial Hospital, and the Department of Medicine, New York University, College of Medicine, New York.

Six drugs which act upon the peripheral vessels probably through different mechanisms have been studied in 6 hypertensive patients adapted to a cool environment (20° C and 55% humidity). Renal blood flow and blood flow to the lower extremities were measured before and after the intravenous administration of the drugs. Hexamethonium, Hydergin, Ilidar and protoveratrine acted similarly in that they were usually followed by an increase in blood flow to the extremity and a simultaneous moderate decrease in renal blood flow. Hexamethonium was, however, the only one which regularly produced a significant fall in arterial pressure in the doses used. In contrast, Apresoline was followed by a slight decrease in blood flow to the lower extremity and a well marked rise in renal blood flow while arterial pressure fell significantly in only one of the three patients studied. Regitine produced no changes in either blood flow or arterial pressure in the dose used (5 mg.).

In the reaction to these drugs, there was a tendency for the renal blood flow and the blood flow to the lower extremities to move simultaneously in opposite directions. In these observations, little correlation appeared to exist between changes in arterial pressure and either blood flow to the kidney or the the lower extremity.

CENTRAL NERVOUS SYSTEM

The Effects of Acute Changes in the Cerebrospinal Fluid Pressure on the Electrocardiogram, Blood Pressure, Pulse and Carotid Sinus Reflex. *Martin S. Belle, Robert Shean,* Morton Halpern* and B. E. Lovenstein,** Miami.

It is not yet clear whether the effects of increased cerebrospinal fluid pressure on the heart are mediated through vagal reflex pathways or by volume receptors in the central nervous system. It has recently been suggested that pre-existing myocardial damage must be present to allow an increase in cerebrospinal fluid pressure to precipitate cardiac failure.

In order to obtain further data on this point, the following series of experiments was done: the cerebrospinal fluid pressure was acutely increased in 7 patients. Six of these had no evidence of myocardial disease; the seventh had luteic aortic insufficiency with left ventricular hypertrophy. Normal saline was instilled into the spinal canal until the pressure was elevated to at least 300 mm. water, and maintained at or above this level throughout the experiment. The electrocardiogram, blood pressure and pulse rates were recorded before and after the spinal fluid pressure was increased, and the effect of ca-

rotid sinus massage was noted. No significant changes were observed in any of the measurements or recordings under increased cerebrospinal fluid pressure.

It is concluded that electrocardiographic changes seen in patients with increased intracranial pressure are not purely reflex in origin. Cardiac decompensation occurring consequent to increased intracranial pressure may be mediated by volume receptors in the central nervous system and probably not alone through vagal reflexes.

Studies on Headache. The Contrast between Cerebrospinal Fluid Pulse Wave Contours during Certain Spontaneous Vascular Headaches and during Headache following Amyl Nitrite and Histamine Administration: Effects of Parenteral Ergotamine. *M. Martin Tunis, Philippe Cardon* and Harold G. Wolff,** Departments of Medicine and Psychiatry, The New York Hospital, Cornell Medical Center, New York.

An electromanometer connected with the lumbar subarachnoid space through a No. 20 needle was used to amplify C.S.F. pulsations. The latter were recorded with simultaneous temporal artery pulse

waves on a multiple channel direct writer. The C.S.F. pulse wave tracings evidenced changes in the contractile state of large intracranial arteries, and were compared with simultaneous alterations in calibre of a representative extracranial artery, usually the right superficial temporal.

This method was employed in 20 normotensive patients with normal C.S.F. pressure to study the vasoconstrictor action of i.v. ergotamine tartrate, 0.25 mg. (11 cases) and the vasodilator effect of amyl nitrite inhalation (6 cases) and histamine infusion 0.1 mg. (3 cases).

During right hemiparesis, a large amplitude right temporal artery pulse wave, with a rounded apex, and outward convexity of the diastolic limb, was recorded. Pulse waves of this type (Tunis, M. M., and Wolff, H. G.: *Am. J. M. Sc.* 224: 565, 1952) were obtained from the involved artery in numerous subjects during vascular headache. Seven minutes after the i.v. administration of 0.25 mg. of ergotamine, pulse wave amplitude was reduced 100% and headache intensity markedly diminished. There was, however, no vasoconstrictor change in the simultaneously recorded C.S.F. pulse waves. Further, when headache-free, the C.S.F. pulse wave tracings were not significantly different from records obtained prior to and shortly following ergotamine therapy for the headache.

During headache induced by amyl nitrite inhalation and histamine infusion, the amplitude of the C.S.F. pulse wave tracings was increased 300 to 600%. When headache subsided, the records returned to the control contour in all instances. Changes noted in the simultaneous temporal artery pulse wave records were often less marked, of shorter duration and at times absent during the headache. As well, there was increased steepness of both the systolic and diastolic limbs of the C.S.F. pulse wave and the contour of the descending limb was concave downward with prompt return to the base line during the headache. These findings indicated dilatation and distention of intracranial vascular structures and decreased vascular resistance.

Extracranial artery pulse waves from the involved vessel during spontaneous migraine headache also evidenced dilatation and distention. By contrast, however, in all instances, there was an outward convexity of the diastolic limb which indicated increased vascular resistance, probably related to intra- and perimural edema of the involved vascular structures.

In short, these pulse wave contour analyses define the differences between headache arising from intracranial arteries (amyl nitrite and histamine) as compared with vascular headache of the migraine type wherein extracranial vessels are the principal source of the head pain.

Thresholds of Response of the Cerebral Circulation to Increases in Blood Oxygen and Carbon Di-

oxide. *John L. Patterson, Jr.,* Albert Heyman and Louis L. Battey,* Emory University School of Medicine and Grady Memorial Hospital, Atlanta.*

Information regarding the minimum changes in blood oxygen and carbon dioxide which affect the cerebral vessels is of physiologic and therapeutic importance.

Inhalation of 100% O₂ was found to produce constriction of cerebral vessels in patients with cerebral vascular disease and may have had deleterious effects in these individuals. Fifty per cent oxygen, approximately the concentration in tents, produced little change in mean cerebral blood flow (CBF) or cerebral metabolism (CMRO₂) in 6 patients with cerebral vascular accidents (CVA).

Administration of 5% CO₂ increases CBF but causes excessive dyspnea, particularly in patients with CVA. Inhalation of 2.5% CO₂ produced little dyspnea but no change in mean CBF, arteriovenous oxygen difference, or CMRO₂. Administration of 3.5% CO₂ was accompanied by slight but tolerable dyspnea, small but statistically insignificant increase in CBF, and decrease in mean cerebral arteriovenous oxygen difference from 6.0 to 5.3 vol.%. Arterial pCO₂ increased 6 mm. Hg, approximately the minimal change for cerebral vasodilator effect.

Inhalation of low concentrations (2.5-3.5%) of CO₂ was followed by apparent increase in motor power within 30 minutes in 7 of 12 patients with CVA. Carbon dioxide in these concentrations may be of value in treatment of patients with early or impending CVA.

A Study Correlating Serum and Cerebrospinal Fluid Electrolytes. *Edward S. Cooper* and Samuel Bellet, Philadelphia General Hospital and the Robinette Foundation, University of Pennsylvania, Philadelphia.*

Little data is available relative to the cerebrospinal fluid (CSF) electrolytes in central nervous system diseases, and especially in the presence of systemic electrolyte imbalance. Serum and CSF electrolytes were determined on 20 normal and 50 abnormal patients. The abnormal cases included acute encephalomalacia (10), cerebral hemorrhage (10), hypertensive encephalopathy (5), tuberculous meningitis (5), and generalized electrolyte imbalance (20).

In the normal patients, the mean CSF potassium concentration was 2.96 mEq./L. and the serum potassium mean was 4.45 mEq./L. The serum and CSF had mean sodium concentrations of 141 mEq./L. and 141.5 mEq./L., respectively. The mean pH of CSF and blood was 7.32 and 7.41, respectively. In cerebral hemorrhage patients, the CSF pH was low with a mean of 7.18, sodium levels were high (without correspondingly high serum levels) with a mean of 154.4 mEq./L. and potassium levels were normal. In generalized electrolyte imbalance cases, high CSF sodium levels accompanied hyperna-

tremia, but low CSF levels did not coexist with hyponatremia. CSF sodium levels were often high without hypernatremia. High CSF potassium levels did not accompany hyperkalemia. Similar and even more striking differences between the serum and spinal fluid potassium values were observed in dogs where hyperkalemia was induced by intravenous administration of this electrolyte.

These data support the concept that the hematoencephalic barrier participates actively in the maintenance of homeostatic balance of the CSF. This was most evident clinically in the failure of CSF potassium to rise as expected in subarachnoid hemorrhage where there was local hemolysis and excessive potassium liberation.

Variations in Ocular Pressure during Electroshock in Humans. *Charles R. Shuman, Robert W. Mather* and Saul Harrison,* Philadelphia.*

Psychiatric patients under treatment with electroshock convulsive therapy were selected for the study of the effect of this procedure upon ocular pressure. Interest in this problem was initiated by the observation of a marked persistent drop in ocular pressure in a glaucomatous diabetic patient following an insulin-induced hypoglycemic convulsion. The patients subjected to electroshock were

free of ocular disease; tonometric readings using pontocaine anesthesia were performed before, during and after the convulsion. Three groups were studied, the first receiving electroshock only, the second given curare prior to the application of the electroshock, the third receiving eserine locally prior to curarization, followed by electroshock.

In the 46 eyes tested of the group receiving electroshock only, a mean fall in ocular tension of 60% was observed within 5 minutes with recovery of preshock tension occurring by 30 minutes. The 14 eyes tested in the curarized group manifested a rapid rise in ocular tension, returning to control levels usually within 5 minutes; no fall in tension below the control levels was observed. The eserinated group consisted of 10 eyes in which the rise observed with curare occurred and was then followed by a fall in ocular tension similar to that seen in the first group.

It is suggested that electroshock produces alterations in cellular and extracellular osmolarity which, in the eye, may affect the osmotic gradient to attract fluid from the aqueous. The role of acetylcholine in furthering these fluid shifts, and the significance of osmotic forces in aqueous humor dynamics are discussed.

COLLAGEN DISEASES—ALLERGY

Serum Glycine Response to Benzoate Administration in Rheumatic Disorders and "Collagen" Diseases. *H. M. Lemon, W. H. Chason* and J. M. Looney,** Evans Memorial, Massachusetts Memorial Hospitals, Departments of Medicine and Biochemistry, Boston University School of Medicine, and the Boston Regional Office, Veterans Administration, Boston.

The response of serum glycine and alanine to administration of 1.77 Gm. sodium benzoate i.v. has been compared in fasted normal patients and those with rheumatoid arthritis, osteoarthritis, gout, rheumatic fever, rheumatic heart disease, scleroderma, discoid and disseminated lupus erythematosus. The fall of serum glycine in excess of 15% of fasting level which has been found to be present in most patients with active rheumatoid arthritis (Lemon, et al.: *J. Clin. Investigation* 31: 993, 1952) has also been noted in patients with hyperuricemia, active rheumatic fever and chronic rheumatic heart disease, and disseminated lupus. No reduction of hepatic or renal function, hippurate excretion, or serum alanine accompanies this response, which is believed to reflect faulty tissue glycine metabolism. These observations indicate one possible common cause for defective collagen and elastin synthesis in rheumatoid arthritis, rheumatic fever and "collagen"

diseases, since these proteins are unique in that glycine constitutes one-third of their amino acid residues.

Alterations in Electrophoretic Patterns in Patients with Rheumatoid Arthritis. *Arthur L. Scherbel and Lena Lewis,** Department of Medicine, Cleveland Clinic, Cleveland.

The effect of treatment on the electrophoretic protein patterns has been studied in 60 patients with rheumatoid arthritis. Electrophoretic patterns (Longworth) were measured at monthly intervals over a period of 6 to 12 months, while the patients received small initial doses of nitrogen mustard and maintenance hydrazide therapy. The patterns were divided into 5 groups on the basis of percentage values of the various protein fractions. Certain of the patterns were observed to return toward normal more promptly than others during the period of treatment. Clinical evaluation of the activity of the disease may or may not coincide with the activity reflected in the electrophoretic patterns.

The drugs used are not specific for rheumatoid arthritis. The observations indicate that a satisfactory response to nonspecific treatment of rheumatoid arthritis is accompanied by a return of electrophoretic patterns toward normal.

Immunologic Studies in Sarcoidosis. *Maurice Sones and Harold L. Israel.* The Woman's Medical College of Pennsylvania, Henry Phipps Institute of the University of Pennsylvania, and the Graduate Hospital of the University of Pennsylvania, Philadelphia.

It has been previously shown that tuberculin-negative patients with sarcoidosis do not respond in a normal fashion to vaccination with BCG. In such patients, tuberculin anergy persists or if allergy results, it is poorly maintained. In order to ascertain the nature of the immunologic defect, patients with sarcoidosis and controls have been subjected to the following: (1) skin tests with other antigens which give a delayed type of reaction (pertussis agglutinin, mumps virus, oidyomyin, trychophytin, and histoplasmin), (2) determination of circulating antibody response and skin reactivity following immunization with pertussis and typhoid-paratyphoid vaccines, (3) passive transfer experiments with ragweed pollen extract, (4) skin reactivity to histamine.

The following results were obtained. Sarcoid patients react significantly less often than controls

to pertussis agglutinin, mumps virus, oidyomyin, and histoplasmin. Study of serum agglutinin titers and skin test responses to pertussis agglutinin indicated inability of the sarcoid group to develop and maintain skin sensitivity, while circulating antibodies developed in a normal fashion. Normal circulating antibody response to intradermal typhoid-paratyphoid immunization was also observed. Passive transfer of ragweed sensitivity was successfully accomplished and cutaneous reaction to histamine injection was entirely normal in sarcoid patients.

The diminished skin reactivity to a variety of agents which produce delayed type skin reactions demonstrates that the tuberculin anergy characteristic of sarcoidosis is nonspecific. The normal circulating antibody response to immunization as well as the normal reaction to histamine, and normal passive transfer responses, demonstrate that the immunologic defect in sarcoidosis is a limited one. Patients with sarcoidosis appear to have a defect in production or transport of antibodies involved in delayed type skin reactions.

ENDOCRINES AND METABOLISM

General Metabolism • Carbohydrate Metabolism • Fat Metabolism Protein Metabolism • Water and Electrolyte Metabolism Adrenal Cortex • Testis • Thyroid • Parathyroid

Metabolic Responses during Prolonged Heat Exposure. *Charles R. Kleeman,* David E. Bass* and Murray Quinn** (introduced by *Edward H. Kass*), Quartermaster Climatic Research Laboratory, Lawrence, Massachusetts, and the Department of Physiology, Boston University School of Medicine, Boston.

Five young men lived continuously under controlled environmental conditions for a 6-week period—a 2-week control period at 75°F., a 2-week period during which the temperature was maintained at 120°F. for 12 hours and at 100°F. for 12 hours of each day (relative humidity 30%), and a 2-week recovery period at 75°F. During the entire 6-week period, metabolic balances of sodium, potassium, chloride, phosphorus, nitrogen and water were determined. Changes in internal balance were calculated at intervals from the metabolic balances, and the previously reported changes in body fluid "compartments" (Bass, Kleeman and Quinn, *Fed. Proc.* 12: 11, 1953). Acclimatization to heat as measured by improved thermoregulation and cardiovascular function occurred in all 5 subjects. The maximum daily sweat losses of water, sodium, potassium and nitrogen seen were 11 liters, 400

mEq., 60 mEq. and 7 Gm., respectively. During the heat exposure periods, mean daily negative balances of 3 Gm. of nitrogen and 20 mEq. of potassium were noted. Sodium and chloride losses calculated from analysis of arm bag sweat concentrations and daily sweat loss lead to apparent mean daily negative balances of 150–175 mEq. This occurred in the presence of an actual expansion of the "extracellular" fluid volume (SCN⁻ space). The losses of body potassium during the heat period were greater than could be accounted for by the negative nitrogen balance and were associated with losses of intracellular water. Daily 17-ketosteroid excretion, basal eosinophil counts and basal total leukocyte counts, in addition to other "indices" of the level of adrenal-cortical activity, showed no significant change from the control period. The implications of these findings and the problems of accurate metabolic balances in prolonged heat exposure will be discussed.

Metabolic Changes during Stressful Life Experiences in Human Subjects. *Basil S. Hetzel,* Daniel S. Lukas, Lawrence E. Hinkle, Jr. and*

Harold G. Wolff,* Departments of Medicine and Psychiatry, New York Hospital-Cornell Medical Center, New York.

Studies of general body metabolism have been carried out by hourly determinations of the serum protein-bound iodine, gaseous exchange and urinary nitrogen excretion before, during and after stressful life experiences in fasting subjects. Two main patterns of change have been observed. During feeling states of tension or depression with steady ventilation, the oxygen consumption is increased in association with a steady R.Q.; the urinary nitrogen does not rise significantly, while the P.B.I. level remains steady. During feeling states of apprehension or anxiety, the oxygen consumption is increased but there is a significant fall in R.Q. with increase in urinary nitrogen excretion and elevation of serum P.B.I. level.

It is provisionally concluded that metabolic adaptation with mobilization of fat and protein stores can occur during certain stressful life experiences in association with an increased output of thyroid hormone.

Some Metabolic Effects of Ethanol in Humans.

David Seligson,* Sheldon S. Waldstein,* Burton Giges,* William H. Meroney* and Victor M. Sborov, Department of Hepatic and Metabolic Diseases, Army Medical Service Graduate School, Washington, D. C.

In an effort to clarify the role of the liver and peripheral tissues in the metabolism of ethyl alcohol, 30 to 70 Gm. were given intravenously to 4 persons (2 normal, 2 patients with hepatic cirrhosis). The infusion time varied from 20 to 120 minutes. Blood for analysis was taken from a peripheral artery, a peripheral vein and the hepatic vein (catheter) before the infusion and at varying intervals thereafter. In all cases there was noted similar but quantitatively different chemical responses.

After ethanol infusion, a metabolic acidosis resulted, manifested by a decrease in pH, plasma bicarbonate and blood buffer base, and by an increase in acetate. Hepatic vein lactate levels, which prior to infusion were lower than the levels in the peripheral artery, increased and exceeded peripheral levels after infusion. Pyruvate, alpha-ketoglutarate, and citrate levels in the hepatic vein decreased following ethanol as did hepatic vein glucose and NPN. Oxygen differences across muscle and liver during alcohol infusion showed no significant changes.

The above data are interpreted to indicate that alcohol is oxidized by dehydrogenation to acetaldehyde and then to acetate. The hydrogen is transported to pyruvate, which forms lactate and leads to a depletion of pyruvate. In turn this results in a depletion of oxalacetate, citrate and keto-glutarate. Since there is insufficient oxalacetate to condense

with it, acetate accumulates and causes acidosis. Infusion of a pyruvate source seems to prevent this acidosis. It is believed that the depletion of the citric acid cycle leads to a decrease in high energy phosphate, which accounts for the reduction of glucose and urea output by the liver.

Contrasting Patterns of Myocardial Metabolism in Diabetes, Cardiac Failure, and after Insulin Administration in Man. Walter T. Goodale, Robert E. Olson and Donald B. Hackel, Department of Medicine, Peter Bent Brigham Hospital and Harvard Medical School, Boston; Department of Biochemistry and Nutrition, University of Pittsburgh; and Department of Pathology, Western Reserve University School of Medicine at City Hospital, Cleveland.

Previously reported coronary catheterization studies in dogs and man have shown excellent correlation between myocardial respiratory quotient, (CO_2 production/ O_2 consumption), and myocardial carbohydrate utilization, (expressed as percentage total myocardial oxygen demand available from equivalent glucose, lactate, and pyruvate extraction). Thus, fasting man showed a myocardial R.Q. of 0.70 ± 0.3 with negligible carbohydrate extraction at low fasting arterial levels, indicating fat utilization. As glucose levels rose postprandially above the myocardial glucose utilization threshold of 56 ± 14 mg.%, pyruvate and lactate levels also rose with correlatively increased myocardial R.Q. and extraction of all three metabolites. Mean postprandial R.Q. was 0.91, confirmed by a carbohydrate extraction which could account for about two thirds of total myocardial oxidation requirements. The remaining third was presumably derived from fat.

In mild diabetes, fasting R.Q. was also 0.7 with markedly reduced or negligible myocardial glucose, lactate, and pyruvate extractions, despite high circulating levels. The glucose utilization threshold was elevated to 95-260 mg.%. Insulin returned this threshold to normal or below, along with marked rises in R.Q. to 1.1-1.2 and with normal or high utilization of all 3 metabolites. These findings tended to confirm the role of insulin in converting carbohydrate to fat. Although diabetes caused defective myocardial carbohydrate utilization, there was no interference with mechanical work or efficiency.

Patients with cardiac failure due to valvular disease, with reduced effective work and efficiency, showed normal lactate and pyruvate and superabundant myocardial glucose extractions, relative to both arterial substrate levels and simultaneous oxygen extraction. Carbohydrate extraction was often sufficient to account at rest for over 150% and on exercise over 200% of simultaneous oxygen extraction. This unaccountable glucose extraction

for nonoxidative purposes is also seen in myocardial tissue slices and other preparations with limited survival time.

There is thus no evidence for anaerobic glucose metabolism nor for myocardial lactate production in the failing heart in vivo. Cardiac failure of this variety thus cannot be related to myocardial anoxia nor to a failure in energy production, but rather to a failure of conversion of chemical energy to effective mechanical work. Paradoxically, the diabetic heart, with limited production of energy from carbohydrate even in mild cases, remains mechanically efficient with energy derived almost entirely from other substrates, such as fat.

Effect of Purified Hyperglycemic-Glycogenolytic Factor (HGF, Glukagon) on Carbohydrate and Corticoid Metabolism in Various Endocrine Disorders. *S. O. Waife, W. R. Kirtley and O. M. Helmer*, Lilly Research Laboratories and the Indianapolis General Hospital, Indianapolis.

Purified pancreatic HGF was administered intravenously (by single injection and infusion) to 17 subjects, including 5 normal controls, 5 unstable and 4 stable diabetics, and 1 subject each with Cushing's syndrome, acromegaly, and hypopituitarism. The following determinations were made at frequent intervals: blood glucose, pyruvate, lactate, potassium, inorganic phosphate, circulating eosinophiles, and hourly urinary 17-hydroxycorticoids, 17-ketosteroids, and creatinine. Epinephrine was administered to some of these subjects for comparison.

In every case a prompt and consistent rise in blood sugar was noted; but, in contradistinction to the effects of epinephrine, blood pyruvate levels did not rise parallel to glucose. Lactate levels in general mirrored the pyruvate response. The blood sugar of stable diabetics did not return to the initial level by 90 or 120 minutes, whereas in the 2 extremely unstable diabetics studied, the sugar returned to fasting levels or even lower. One acromegalic with diabetes whose blood glucose and pyruvate did not rise following epinephrine administration showed a typical glycemic response to HGF.

Serum potassium levels were essentially unchanged. Serum inorganic phosphate levels tended to fall, but to a lesser extent in diabetics. Circulating eosinophiles did not show a consistent change in 3 hours.

Whereas there was a significant transient increase in the urinary 17-hydroxycorticoid/creatinine ratio in both normal and diabetic subjects in the hour immediately following HGF administration, in a patient with hypopituitarism (exhibiting diminished adrenal function) HGF caused the expected change in carbohydrate metabolism without an increase in steroid excretion. This suggests that the hyperglycemic action of HGF is independent of the pituitary-adrenal axis.

A comparison of the effect of various hormones on certain aspects of carbohydrate metabolism is discussed.

A Comparison of Insulin Treatment with and without Added Carbohydrate in Human Diabetic Ketosis. *Marvin Rosecan* and William H. Daughaday*, Washington University School of Medicine, St. Louis.

A controversy exists whether the administration of carbohydrate to patients in diabetic acidosis actually speeds recovery from ketosis. To study this problem the fall of blood ketones during insulin therapy with and without the addition of carbohydrate has been compared. A direct comparison was made possible by inducing ketosis 15 times in 5 patients by insulin withdrawal for 1 to 3 days. Initial blood ketone levels averaged 5.1 mM./L. Insulin dosage (average, 50 units) was constant for all studies on any one patient. Glucose or fructose or comparable volumes of saline were administered intravenously (0.8 Gm./Kg./hr.) for 4 hours. Blood levels and urinary excretion of total ketones, glucose, and fructose were followed for 6 hours.

With insulin and saline (5 patients) blood ketones fell from 4.6 mM./L. to 3.1 mM./L. With insulin and fructose (5 patients) blood ketones fell from 5.9 mM./L. to 2.7 mM./L. With insulin and glucose (3 patients) blood ketones fell from 5.2 mM./L. to 1.8 mM./L. Analysis of the results indicate that addition of carbohydrate to insulin in the treatment of diabetic ketosis results in a significantly faster fall of blood ketone levels. No superiority of fructose over glucose in respect to rate of decrease in ketonemia could be demonstrated in this small series.

The total blood reducing sugar was significantly higher when insulin and glucose were used as compared to insulin and fructose. When fructose was given, 78% of administered carbohydrate was retained as compared to 32% when glucose was given.

Studies in Experimental Diabetic Acidosis: Effect of Therapy with Glucose and Fructose on Water and Electrolytes. *J. R. Murphy, J. W. Craig, Max Miller, H. Woodward* and S. Levey*, School of Medicine, Western Reserve University, Cleveland, Ohio.

There is considerable disagreement concerning the use of carbohydrate in the treatment of diabetic acidosis. Many authors state that early administration of glucose results in increased glycosuria and loss of electrolytes. Treatment with fructose, glucose and without carbohydrate was compared in the same patient in 3 episodes of acidosis, the remainder of therapy being kept constant. Diabetic acidosis with blood ketones over 50 mg. % developed in 42 to 47 hours after insulin withdrawal. Treatment for the first 6 hours included 350 units of insulin and 3300 ml. of saline in each episode, 175

Gm. of fructose in the first, 175 Gm. glucose in the second, and no carbohydrate in the third.

During development of acidosis, marked deficits of water, sodium, potassium and chloride occurred. Treatment with 175 Gm. of fructose as compared with treatment without carbohydrate at similar initial blood sugar levels did not result in an increased urine volume or loss of electrolytes. The same amount of glucose at a lower initial blood sugar level resulted in similar urinary excretions. In all cases there was a continued loss of water from the cell during the first 6 hours of treatment. Potassium entered the cell in this period when fructose was given but shifted out when glucose or no carbohydrate was given. When fructose was given the blood sugar decreased earlier than with glucose and slightly later than without carbohydrate. The use of carbohydrate early in treatment resulted in assimilation of significantly greater amounts, being most marked with fructose.

Insulin Sensitivity in Diabetic and Nondiabetic Individuals. *Alvin E. Parrish and Louis K. Alpert, Veterans Administration Hospital, Washington, D. C.*

Insulin sensitivity in diabetic and nondiabetic patients was tested by administering small amounts of insulin intravenously to patients receiving intravenous glucose at a constant rate. Preliminary studies demonstrated that, when glucose was given at a constant rate, the blood sugar stabilized at an elevated level in 30 to 60 minutes, and remained so for periods up to 2.5 hours. When insulin was given during this stable period, the subsequent fall in blood sugar served as a test of insulin sensitivity. In the diabetic patients, the slope of the blood sugar curves following intravenous injection of insulin were calculated and compared. These slopes ranged from 0.1 mg./min. to 6.0 mg./min. fall in blood sugar, the average being 1.7 mg./min. There was no sharp delineation into separate groups and in the small group of patients studied, appeared to resemble the distribution curve of a normal population. This suggests that diabetic patients cannot be divided sharply into insulin resistant and sensitive groups.

Blood pyruvate levels were also determined, and the curves observed could be classified into two groups: (1) those in which there was a rise in pyruvate concentration followed by a fall within 60 minutes, and (2) those in which there was a continued rise in pyruvate level which was continuing at the end of 60 minutes. In general, the latter type of curve was associated with the less sensitive responses to insulin.

In the nondiabetic patients the rate of fall of the postinsulin blood glucose levels was similar to that of the diabetic individuals. The blood pyruvate curves were also similar in the two groups of patients.

These observations suggest that the sensitivity of diabetic patients to insulin does not differ materially from that of nondiabetic individuals.

The Fall in Serum Inorganic Phosphorus and Potassium Levels in Normal and in Diabetic Individuals following the Intravenous Injection of Glucose. *Marcel Roche,* Francisco de Venanzi* and Jorge Vera* (introduced by Peter H. Forsham), Caracas, Venezuela.*

One ml. per kilo of body weight of a 50% glucose solution was administered intravenously to 31 normal individuals and to 17 diabetic patients in the resting, fasting state. Blood sugar (Somogyi-Nelson), serum inorganic phosphorus (Fiske and Subbarow) and potassium (Beckman DU flame photometer) were determined before and 15, 30, 45 and 60 minutes after the injection of glucose. The average maximum fall in the normal was 0.93 mg. % (S.E. 0.11) for phosphorus and 0.48 mEq./L. (S.E. 0.07) for potassium; in the diabetic 0.46 mg. % for phosphorus (S.E. 0.07) and 0.72 mEq./L. (S.E. 0.06) for potassium. The difference in phosphorus fall between normal and diabetic individuals proved statistically highly significant, whereas the difference for potassium was of only moderate significance ($t = 1.91$).

The results suggest strongly, however, that the relation between potassium and carbohydrate metabolism is fundamentally altered in diabetes, and that this alteration is not directly related to the fall in serum inorganic phosphorus upon the infusion of glucose.

Further Studies in Experimental Mouse Obesity. *William Parson, K. R. Crispell, James Camp,* Department of Internal Medicine, School of Medicine, University of Virginia, Charlottesville.*

Previous studies have revealed an abnormal response to 50% dietary dilution with Kaolin in experimental mouse obesity produced by the injection of gold thioglucose (L.D. 60). Further studies indicate that during the ascending phase of the experimental obesity as well as during the plateau phase, the obese mice do not respond, as control litter mates do, to dietary dilution, with a prompt increase in the volume of the food ingested so that the weight curve is unaffected. The obese mice respond slowly and inadequately and lose weight.

Kennedy has described a similar abnormal response to dietary dilution in experimental rat obesity produced by electrolytic lesions in the hypothalamus during the "plateau" phase and not during the "ascending" phase. This discrepancy with our findings is of considerable theoretic interest, and will be discussed.

The dietary behavior in response to increased caloric needs was studied by thyroxine adminis-

tration. Daily intraperitoneal injections of 25 gamma l-thyroxine to control litter mates resulted in increased food ingestion and no significant weight change. The experimentally obese mice responded with an inadequate increase in food intake and lost weight.

Our working hypothesis is that the hyperphagia of the obese animals is a resultant of 2 homeostatic defects: A serious interference with the mechanism of stopping eating, "the satiety mechanism," and a less serious interference with the "mechanism of hunger."

The Effect of ACTH and Certain Adrenal Steroids on Total Body Fat with Observations on the Specific Gravity Technic. *Paul D. Doolan, Walter C. Welum* and Laurence H. Kyle.* The Department of Medicine, Georgetown University School of Medicine and the Experimental Diving Unit, U. S. Naval Gun Factory.

Studies were conducted on 4 patients in an attempt to learn whether adrenal steroids increased total body fat. Each subject was given a constant diet and the urinary nitrogen excretion measured daily. Total body fat was measured by the specific gravity method described by Behnke, which is accurate to within ± 0.003 units. Other studies included serial measurements of the blood total lipids, phospholipids, cholesterol, amino nitrogen, pyruvic acid glutathione, and total eosinophiles as well as the excretion of 17 keto- and formaldehyde-steroids.

In a patient who received ACTH the specific gravity rose four units, indicating some loss of body fat. There was no change in specific gravity in the patient given cortisone. In both cases, hyperadrenal (Cushinoid) states were induced, accompanied by changes in body composition due primarily to variations in water content.

No significant clinical biochemical or specific gravity changes were observed in a patient given Compound A. There was a significant fall in specific gravity in a patient who received Compound F, indicating an increase in body fat. During treatment, however, the urinary nitrogen excretion had increased and the change in specific gravity may therefore have been due to a decrease in lean body mass.

Comparatively little clinical use has been made of the specific gravity technic. Although it serves as an accurate measure of total body fat in normal subjects, this study demonstrates that under conditions of abnormal or changing body composition, direct measurements of other body components must also be made before quantitatively precise estimations of the changes in fat content can be deduced from specific gravity data.

Essential Hyperlipemia: Effects of Dietary and Hormonal Factors on Serum Lipids. *Stefan S.*

Fajans, Laurence H. Louis, Henry D. Kaine and Jerome W. Conn,* Ann Arbor.*

The study was carried out to determine whether changes in dietary fat per se or alterations in total caloric intake are responsible for variations in concentration of serum lipids in essential hyperlipemia. In 2 patients with severe essential hyperlipemia, reduction of dietary fat with or without caloric restriction caused a sharp fall in concentration of serum lipids (total fatty acids, neutral fat, phospholipids, cholesterol, and ester). An increase in dietary fat, with or without caloric restriction, produced a pronounced rise in serum lipids.

The female patient had a secondary eruptive xanthomatosis and also coexisting hypothyroidism. She had experienced a remission of her xanthomatosis during pregnancy and an acute exacerbation 3 days after delivery. This patient, while on a diet which maintained hyperlipemia, exhibited a rapid fall in the concentration of neutral fat and cholesterol upon the administration of ACTH for 5 days. A rebound rise was observed following discontinuation of ACTH. Large doses of stilbestrol caused an increase in concentration of serum lipids and an intense exacerbation of the xanthomatosis. Administration of thyroid was associated with a minimal fall in concentration of serum lipids. It seems likely that the spontaneous remission of the xanthomatosis during pregnancy was not due to the rise in estrogen levels but rather due to the increase in corticoids which occurs during pregnancy.

It is concluded that dietary fat rather than total caloric intake is the critical factor in lowering or raising the concentration of serum lipids in essential hyperlipemia.

The Metabolism of Labeled Cholesterol in Normo- and Hypercholesterolemic Man. *Leon Hellman,* Robert Rosenfeld,* and T. F. Gallagher,* Sloan-Kettering Institute for Cancer Research; Chun-I. Wang* and David Adlersberg, Mount Sinai Hospital, New York.*

Cholesterol-4-C¹⁴ was fed to 3 patients exhibiting the typical clinical and biochemical signs of idiopathic hypercholesterolemia (primary essential xanthomatosis) and to 2 patients with normal plasma cholesterol levels. The specific activity of the plasma-free and ester cholesterol was studied at intervals for approximately 100 days. The absorption and excretion of ingested cholesterol was followed by examination of the radioactivity in urine and stool. From 25-60% of the administered radioactivity was recovered in the feces and 0.5-2.5% appeared in the urine over a period of 10 to 14 days. No radioactivity appeared in the expired CO₂.

Higher levels of radioactivity appeared sooner in the plasma-free cholesterol than in the ester cholesterol. Peak specific activity of the free cholesterol was reached in 0.8 to 2 days and the maximum ester activity occurred later at 2 to 3 days.

At the time the maximum level of radioactivity was attained, 15-25% of the administered cholesterol was in the circulating plasma. The specific activities of the free and ester cholesterol were equal only at the peak of the ester activity. After that point, the ester radioactivity declined but continued to exceed the specific activity of the free cholesterol for periods of 3 to 4 months. This suggests that the pool of ester cholesterol is physiologically distinct from that of the free cholesterol. Mathematical analysis of the relationship between the free and ester cholesterol radioactivity curves indicates that free cholesterol is a direct precursor of ester cholesterol.

The data obtained by this method of study fail to disclose any apparent difference in the turnover of plasma cholesterol in patients with essential hypercholesterolemia as compared to the control subjects.

The Effect of Heparin on the Formation of P^{32} -Labeled Phospholipid. *Walter J. Levinsky, Philadelphia.*

A total of 11 patients was given P^{32} , of whom 5 received heparin at the time of administration of the tracer dose and 6 served as controls. Subsequently, 4 patients with coronary insufficiency were given P^{32} with heparin. Blood was withdrawn at 6, 12, 24, 48, and 72 hours after the tracer dose.

Although heparin is capable of producing alterations in the blood lipoprotein spectrum, it did not significantly alter the specific activity versus time curves of phospholipid in normal and coronary arteriosclerotic patients as measured by the P^{32} tracer technic. Measurement of the newly formed phospholipid in a group of control patients gave specific activity values which were similar over a 72 hour period to those obtained in heparin-treated patients.

It will be necessary to obtain additional data relating to the turnover rate of phospholipid, by studying the specific activity curve within the first 12 hours after the injection of P^{32} .

Evaluation of Radioactive Iodinated Human Serum Albumin as a Tool in the Study of Protein Metabolism Following Severe Thermal Trauma. *William C. Levin, William R. Hurst* and T. G. Blocker, Jr.,** Departments of Medicine and Plastic and Maxillofacial Surgery and the Hematology Research Laboratory, The University of Texas Medical Branch, Galveston. (Supported by U. S. Public Health Grant #G-3561.)

In an effort to obtain precise data with regard to the utilization of concentrated protein feedings in patients with severe burns, studies have been made on the absorption and urinary excretion of orally administered human serum albumin tagged with radioactive iodine. Using a technic described

in a previous report, 50 to 100 microcuries of labeled albumin mixed with powdered Protenum (1 Gm. per Kg. of body weight) and diluted to 240 cc. with whole milk were fed to patients previously prepared with Lugol's solution. Percentage of radioactivity in circulating blood plasma and in the urine was determined (using a Geiger-Muller tube) at regular intervals following ingestion of the material. Results in 14 burn patients (with over 20% body surface involvement) have been compared with those in 48 patients without obvious metabolic disturbances.

In all patients, the maximum concentration of activity was observed at the end of 3 hours. One hour after administration of the material, concentration in the plasma was essentially the same in both normal and burn patients; but, although the absorption curves showed the same configuration thereafter with a gradual plateau-like decrease, the burn group demonstrated significantly lower levels at 3 and 6 hours. There was also a corresponding increase in the rate of urinary excretion during the first 24 hours as compared with normal patients. These findings probably reflect an increased metabolic rate following severe thermal trauma.

Studies carried out in normal patients with sodium iodide labeled with I^{131} show about the same concentrations of activity as in the control group above, although lower levels were generally observed. It would appear, therefore, that the use of orally administered radioactive iodinated human serum albumin is not a valid method for studying protein metabolism per se.

Quantitative Estimation of Glutamic-Oxaloacetic Transaminase Activity in Human Serum. *Arthur Karmen,* Felix Wroblewski and John S. LaDue, Memorial Center for Cancer and Allied Diseases, New York.*

Studies of the transamination reaction in various animal tissues reveal that glutamic-oxaloacetic transaminase activity is found in varying concentration in such tissues as liver, kidney, skeletal muscle and others. The enzymatic activity is, however, greatest in cardiac muscle. To determine whether changes in cardiac muscle metabolism could be reflected in the enzymatic content of the extracellular fluid, it was of interest to measure this enzyme activity in human peripheral blood. By adapting a method for the quantitative chromatographic analysis of amino acids to the determination of minute enzymatic activity, glutamic oxaloacetic transaminase activity was demonstrated in human peripheral blood. The distribution of the activity in the components of blood and the physicochemical characteristics of the enzyme as found in serum were determined. Measurement of the activity in the serum of normal persons was made, and the range of normal activity ascertained.

N^{15} Excretion Rates following Oral and Intravenous Administration of N^{15} Glycine to Normal Subjects and Patients with Cushing's Syndrome on Low, Intermediate, and High Protein Diets. William Parson, K. R. Crispell and Gardner Harden,* Department of Internal Medicine, School of Medicine, University of Virginia, Charlottesville.

Normal subjects and patients with Cushing's syndrome were studied during metabolic periods in nitrogen equilibrium while on low protein (25 Gm./Kg.), normal protein (1.0 Gm./Kg.), and high protein (1.5 to 2.5 Gm./Kg.) diets. Following a period on each of these dietary regimes, a single dose of glycine tagged with N^{15} was administered orally or intravenously.

The excretion rates of N^{15} following oral administration as compared with intravenous administration revealed the following: The normal subjects on the normal protein intake excreted in 24 hours 23-28% (orally tagged) and 13-18% (intravenously tagged). On a low protein diet the excretion rate in 24 hours fell to 8% (orally tagged) and 4-5% (intravenously tagged). The high protein diet increased the excretion rate in 24 hours to 45% (orally tagged) and 30-33% (intravenously tagged).

In 3 patients with Cushing's syndrome in nitrogen equilibrium, tagged orally on the normal diet, the excretion rate in 24 hours was from 45-51%. On the low protein diet the excretion rate fell to 28 and 39% in one subject. On the high protein diet the excretion rate was 47 and 51%.

This technic offers a useful method to study dietary protein requirements. It has been shown that a regime of "excess" dietary protein results in an increased rate of degradation and excretion of orally or intravenously administered amino acids. Other possible effects will be discussed.

The data suggest further that a high protein diet in Cushing's syndrome ameliorates the apparent increased rate of degradation of ingested amino acids and decreased protein synthesis.

The Inhibition of Lysozyme by Heparin. Grace P. Kerby and G. S. Eadie,* Departments of Medicine and of Physiology, Duke University School of Medicine, Durham.

The function of lysozyme in mammalian fluids and cells has never been known. The presence of the enzyme has been demonstrated in the past by its lytic effect on certain micro-organisms and by its alteration of the viscosity of a mucopolysaccharide derived by Meyer from micro-organisms. Investigation of the possibility of a primary metabolic function concerned with depolymerization or hydrolysis of a similar substrate in mammals has been hampered by the failure to identify the substrate in extracts of various organs.

In the present study, heparin in final concentration of 10 mg. per ml. has been shown to in-

hibit crystalline egg lysozyme (1 μ g. per ml.), a dried preparation of *M. leisodeikticus* being used as substrate over a range in concentration of 180 to 48 mg.%. By the usual criteria set forth in the Michaelis-Menton formulation, the inhibition is competitive.

This demonstration of competitive inhibition of lysozyme by an acid mucopolysaccharide of composition similar to several well-recognized components of certain mammalian tissues emphasizes the need for further intensive search for a substrate for lysozyme in those tissues where the enzyme is present in high concentrations.

Water Retention and the Antidiuretic Hormone in Hepatic and Cardiac Disease. Abraham G. White, George Rubin* and Louis Leiter.* The Medical Division, Montefiore Hospital, New York.

An infusion of 5% glucose in water was administered intravenously at 10 cc. per minute to 7 control subjects, 10 cardiacs, and 5 patients with liver disease (4 with decompensated liver cirrhosis and 1 with infectious hepatitis), and the resulting water diuresis studied. While the glucose infusion continued and after the urine flow reached a plateau, 0.57 mU/Kg. of Pitressin was injected intravenously into the 7 controls, into 6 of the cardiac patients and into the 5 hepatic patients.

Following onset of the infusion the average time required for attainment of peak diuresis in the control subjects, cardiac patients, and liver patients was: 85.1 ± 32.3 , 99.1 ± 32.1 , and 88.6 ± 27.2 minutes, respectively. The average peak urine flows attained during the hydration periods were: 12.0 ± 2.7 , 6.7 ± 3.3 , and 11.9 ± 3.0 cc./minute for the 3 groups.

There was no significant difference in the duration of, and intensity of, Pitressin antidiuresis under these experimental conditions in 3 groups of patients, except for one of the cardiacs who demonstrated an enhanced water antidiuresis. In the dosage administered, Pitressin did not exert any significant effect on the urinary output of sodium, chloride or potassium. As for the effect of Pitressin on the concentrations of electrolytes in the serum, it was noted that the only consistent change was that of the serum sodium which tended to fall during Pitressin antidiuresis in the 5 patients with liver disease.

In summary, these data offer no conclusive evidence for any deficiency in the mechanisms of inactivation of Pitressin administered in physiologic dosage to controls, cardiacs or patients with liver disease.

The Availability of Bone Sodium. G. Nichols, Jr., and N. Nichols, U. S. Submarine Base, New London, Conn.

Rapid losses of body sodium cause, initially,

no change in plasma sodium concentration. Later, low plasma sodium, acidosis and shock ensue. This study was undertaken to determine (1) the source of the sodium that sustains extracellular fluid levels in the early hours of acute sodium loss, (2) rate of availability of this sodium, and (3) total amount available.

A pure sodium deficiency was produced in 11 dogs by means of dialysis. 70-200 mEq. of sodium were removed from each animal. In dogs dialysed for 6 hours, plasma sodium concentrations fell an average of 16.6 mEq., or 2.8 mEq./hour. Plasma pH was unchanged at 3 hours and fell to acidotic levels between 3 and 6 hours. CO₂ dropped rapidly between 0 and 3 hours and more slowly between 3 and 6 hours. Blood pressure fell rapidly between 4 and 6 hours. Intracellular muscle sodium was unchanged at 3 and 6 hours. Bone sodium decreased an average of 18.6 mEq./Kg. wet bone during the dialysis; 75% of this drop occurred between 0 and 3 hours.

It would appear that 12-15 mEq. (average: 13.7) of sodium/Kg. wet bone can be mobilized at a rate of 3-5 mEq./hour. After this, the rate of availability of bone sodium declines to 1-2 mEq./Kg. wet bone/hour, and collapse of the extracellular structure, acidosis, and shock ensue. Assuming bone to comprise 18% of body weight, an acute loss of sodium in excess of 2 mEq./Kg. body weight will result in acidosis and shock.

Effect of DCA and Cortisone on Electrolyte Excretion in Adrenalectomized Dogs with Thoracic Inferior Caval Constriction and Ascites. *James O. Davis and David S. Howell*, Laboratory of Kidney and Electrolyte Metabolism, National Heart Institute, National Institutes of Health, Public Health Service, Federal Security Agency, Bethesda.

Ascites formation in dogs is characterized by (1) a reduction in urinary Na and K excretion, (2) decreased fecal Na output, and (3) an elevation in fecal K excretion. This pattern of electrolyte excretion disappears following bilateral adrenalectomy during maintenance on 0.5 mg./day of DCA and ascites ceases to accumulate. The present observations with DCA (0.5-25.0 mg./day) and cortisone (20-70 mg./day) were made to determine the efficacy of these hormones in producing this abnormal pattern of electrolyte excretion. It was found that the degree of Na retention was proportional to the amount of DCA administered and only large doses of DCA (10-25 mg./day) effected complete replacement; the low level of urinary and fecal Na excretion, the reduced urinary K output, and the elevated rate of fecal K excretion reappeared. The data suggest that an excess of adrenocortical salt retaining hormones is present during the abnormal electrolyte excretion characteristic of ascites formation in dogs with intact adrenal cortices.

Since the number of circulating eosinophils is not detectably altered during ascites formation, cortisone was administered to determine its salt-retaining action. Salt retention failed to occur at any dosage level of cortisone employed. The animals diuresed completely and remained in excellent health.

It appears, therefore, that DCA-like hormones rather than 11,17-oxysteroids are essential to ascites formation.

Blood Volume and Extracellular Fluid Volume during Administration of ACTH and Cortisone. *Mackenzie Walser, Donald W. Seldin and Charles H. Burnett*, Southwestern Medical School of The University of Texas, Dallas.

The relationship between expansion of extracellular fluid volume (ECF), blood volume, and salt excretion was examined in normal subjects given large doses of ACTH and cortisone with and without dietary salt.

During salt restriction (10-12 mM. NaCl/day) ACTH and cortisone produced slight increases in blood volume (T-1824 or P³²-labelled erythrocytes) and ECF (radiosulfate space). Balance data showed that the increments in ECF were greater than could be attributed to retention of dietary salt.

When 10 Gm. of salt daily were added to the diet, administration of ACTH or cortisone resulted in 3-4 liters expansion of ECF, coincident with large positive balances of sodium and chloride. Nevertheless, plasma volume did not increase and failed to reflect day to day variations in ECF. Peripheral venous pressure rose only slightly, and serum proteins showed no significant change. After withdrawal of hormone, ECF returned to control values while plasma volume remained constant.

ACTH or cortisone may produce sustained expansion of the interstitial fluid without augmenting blood volume. The stimulus which promotes renal adjustment to an excess of extracellular fluid evidently need not involve blood volume, venous pressure, or plasma oncotic pressure.

Nucleic Acid Changes in Tissues of Normal and Diphtheria-Intoxicated Guinea Pigs Treated with Cortisone. *Leon T. Atlas*, Department of Medicine, Harvard Medical School; Peter Bent Brigham Hospital, Boston.

In preliminary studies it was established that cortisone in adequate dosage significantly delays the lethal effect of diphtheria toxin on guinea pigs. The contents of nucleic acids in samples of liver, kidney, spleen, heart and adrenal from normal animals and groups receiving diphtheria toxin alone, diphtheria toxin with cortisone therapy and cortisone therapy alone were compared. It was found that diphtheria toxin alone reduced the ribonucleic acid content per unit dry weight of most of the tissues studied. This significant reduction occurred per

unit cell in liver. Cortisone alone produced a significant reduction of total nucleic acid content per unit dry weight of liver, kidney, spleen and adrenal in normal animals. In all these tissues, cortisone alone reduced the ribonucleic acid content to some extent.

Cortisone produced a significant reduction of desoxyribonucleic acid content of liver, both per unit dry weight (15%) and per unit cell (14.7%). In liver and kidney, and to a lesser extent in other tissues, cortisone therapy decreased the magnitude of the loss of ribonucleic acid content effected by diphtheria toxin. The morphologic findings were consistent with these results. Cortisone produced a marked reduction of the characteristic morphologic changes in tissues of guinea pigs receiving diphtheria toxin. These data suggest that cortisone may have a basic mode of action on nucleic acid synthesis or breakdown. This unknown mechanism alters the effect of diphtheria toxin on the nucleic acid contents of cells and increases the longevity of such cells.

Relative Adrenal Insufficiency. *Harold Brown, Avery A. Sandberg,* Don H. Nelson* and Frank H. Tyler, Veterans Hospital and Departments of Medicine and Biochemistry of the University of Utah College of Medicine, Salt Lake City.*

Many acute and some chronic clinical phenomena have been presumed to be the result of functional impairment of the adrenal cortex. However, attempts to prove the adrenal factor in such patients have been virtually impossible. On the other hand most patients with Addison's disease have obvious findings, both clinical and biochemical which make their identification simple. The development of a technic for the quantitative estimation of 17-hydroxycorticosteroids in small amounts of plasma has clarified at least one aspect of this problem. The majority of patients with clinically typical Addison's disease have no detectable steroid by this technic. However, 2 patients who developed Addisonian-like symptoms with infections were found to have circulating 17-hydroxycorticosteroid levels within the normal range both during and after the episodes of clinical "adrenal insufficiency." Normal amounts of 17-hydroxycorticosteroid were excreted in the urine. The administration of corticotropin (ACTH) to these patients did not change the circulating 17-hydroxycorticosteroid, eosinophil or lymphocyte levels. In contrast, epinephrine produced good decreases in the circulating eosinophils but did not significantly change the steroid levels. Neither patient had experienced hypoglycemic symptoms and oral glucose tolerance tests were normal. At autopsy one of the patients had extensive but not complete destruction of his adrenals by tuberculosis as well as disseminated tuberculosis. These findings are consistent with the hypothesis that the patient's remaining adrenal-cortical tissue

was functioning maximally and maintaining eucorticism under basal conditions. With an acute infection he developed relative hypocorticism. It seems apparent that "relative adrenal insufficiency" can exist in this very special anatomic circumstance.

Plasma Clearance of Neutral 17-Ketosteroids.

Lyll I. Gardner, Department of Pediatrics, State University of New York, Medical School at Syracuse.

Plasma concentrations of neutral 17-ketosteroids have been found to approximate 50 $\mu\text{g.}\%$ in normal man and as high as 220 $\mu\text{g.}\%$ in congenital adrenal hyperplasia. In the adult male plasma clearances of these steroids are about 25 ml./min./1.73 sq.m. and in congenital adrenal hyperplasia 110 ml./min./1.73 sq.m. In the latter disease state, plasma 17-ketosteroid clearance closely approaches glomerular filtration rate in the face of marked endogenous overproduction of 17-ketosteroids. It is postulated that plasma 17-ketosteroids in normal men pass into the glomerular filtrate and are in part reabsorbed by the tubule, but are not excreted by the tubule.

In untreated congenital adrenal hyperplasia there appears to be maximal glomerular filtration of 17-ketosteroids with nearly complete inhibition of tubular reabsorption.

Bioassay of Adrenal Corticosteroids and Human Urinary Corticoids by Effect on Sodium and Potassium Excretion. *Ben B. Johnson* and John A. Luetscher, Jr.* (introduced by Robert Commons), Stanford University School of Medicine, San Francisco.*

Previous work has shown increased sodium-retaining activity in urine extracts from certain patients with edema and from normal men with severely restricted sodium intake. Similar extracts of normal urine have no significant sodium-retaining activity by bioassay in adrenalectomized rats. A bioassay method has been developed to characterize the known active adrenal steroids and the sodium-retaining urinary corticoid fraction. Sodium, potassium and water excretion are measured in the water-loaded adrenalectomized rat. Measurements after injection of the substance to be assayed are compared with the effect of a DOCA standard and a solvent control in the same rat, on different days. The sodium output gives a qualitative differentiation between the 11-desoxycorticosteroids (DOC) and 17-hydroxy-DOC, which cause sodium retention, and the active 11-oxysteroids such as cortisone, which increase sodium excretion. The potassium output is increased by adequate doses of all the known biologically active adrenal corticosteroids, and the K/Na output ratio gives more accurate quantitative estimation of doses of DOCA in the 5 microgram bioassay range. Water excretion is

greatly enhanced by the 11-oxysteroids. A dosage-response curve with known statistical variance has been established for sodium-retaining steroids.

The bioassay technic has been applied to paper chromatographic fractions of urinary corticoids. Abnormal sodium-retaining activity found in certain urine extracts was quantitatively recovered in a fraction distinct from known sodium-retaining adrenal steroids. This fraction caused increased potassium excretion in the bioassays. The sodium-retaining corticoid measured in urine resembles in chromatographic behavior and in high specific activity the mineralocorticoid observed by Grundy, Simpson, Bush and Tait in beef adrenal cortical extract and in mammalian adrenal vein blood. Further studies are in progress on the nature of the active material, using the bioassay method as a guide.

Endogenous Testosterone Inhibition as a Method for Comparing Exogenous Testosterone Esters in Terms of their Effects on Urinary 17-Ketosteroid Excretion. *R. Palmer Howard, Henry H. Turner,* Edward C. Reifstein, Jr., and Burton S. Lowrimore,** The Section on Endocrinology and Metabolism, Oklahoma Medical Research Foundation, and the Department of Medicine, University of Oklahoma School of Medicine, Oklahoma City.

The testosterone produced by the human testis is one of the sources of the urinary 17-ketosteroid metabolites. Administered testosterone appears, in part, as an increment to these urinary compounds. The duration of the increase in excretion has been used by other investigators and by the authors (in 5 patients) to compare the effect of various testosterone esters. Thus, it has been shown that testosterone cyclopentyl propionate (TCP) and testosterone phenyl acetate (TPA) have a more prolonged effect than testosterone propionate (TP). There are difficulties in employing this procedure due to the spontaneous daily fluctuations in the urinary 17-ketosteroid level of each individual.

Previous studies by one of the authors have shown that 17-methyl testosterone not only is not excreted as 17-ketosteroid metabolites, but actually leads to a reduction in the 17-ketosteroid excretion, probably by inhibiting the endogenous testosterone production.

This fact has been utilized in the present investigation to stabilize the daily 17-ketosteroid excretion. Five patients were given 17-methyl testosterone daily (75 to 200 mg. per day) until their daily excretion levels were reasonably consistent. Single large doses of equivalent testosterone content of TCP, TPA, and TP were then injected separately at suitable intervals and the 17-ketosteroid excretion determined. The oral administration of methyl testosterone was continued throughout. The daily increment and the total excretion attributable to

the injected steroids was determined. Again TCP and TPA exhibited a more prolonged effect than TP.

The evidence suggests that the enzymatic systems by which testosterone esters are metabolized to 17-ketosteroid excretory products are able to function adequately in the presence of large amounts of methyl testosterone.

The Study of Thyroid Function by Means of a Single Injection of Thyrotropin. *Richard P. Levy,* Luther W. Kelly, Jr.,* and William McK. Jeffries, Cleveland.*

Current tests of thyroid function serve to reflect the activity of the gland at the time of the procedure, but give no indication of its ability to respond to stimulation, i.e., thyroid reserve. A study in normal individuals indicates that a single intramuscular injection of thyrotropin (TSH) in a dose as small as 10 mg. produces a significant increase in serum protein-bound iodine (PBI) and thyroidal uptake of I^{131} within 24 hours. Patients with primary hypothyroidism show no such response. A patient with panhypopituitarism had a low initial uptake of I^{131} , but responded well to this dose of TSH.

The administration of thyroid extract to normals causes a decrease in the initial I^{131} uptake, but response to TSH is not inhibited. Iodide obscures the uptake of I^{131} both before and after TSH, but an increase in PBI still occurs. Hence, neither thyroid extract nor iodide blocks TSH effect on the thyroid gland, and it is possible to determine thyroid reserve in spite of the administration of either of these substances.

After subtotal thyroidectomy or I^{131} therapy for hyperthyroidism, patients may show normal initial levels of these two indices, but poor response to stimulation by TSH, a finding consistent with decreased thyroid reserve in the residual tissue. Cases of ophthalmopathic Graves' disease may or may not have normal responses to TSH.

These studies indicate that a single injection of a comparatively small dose of TSH can be used to study thyroid function in a manner which has not previously been possible.

Use of Radioactive Iodine (I^{131}) Uptake in the Diagnosis of "Masked" Hyperthyroidism in Patients with Auricular Arrhythmias. *Richard P. Mueller and Brown Dobyns* (introduced by S. M. Sances), Cleveland.*

This is a preliminary report on the thyroid function, as measured by the radioactive iodine (I^{131}) uptake, in 100 patients with auricular arrhythmias with or without clinical evidence of organic heart disease.

This was done in addition to the usual laboratory and clinical observations used to evaluate thyroid function, and served as a method for

the identification of hypermetabolism in patients with cardiac abnormalities.

In 20 of the 100 patients there was evidence of "excessive thyroid function" as shown by I^{131} uptakes. An uptake of 55% of the dose of I^{131} after 48 hours was regarded as evidence of "excessive thyroid function." In nodular goiters the demonstration of excessive concentration of I^{131} in a single nodule by directional counting gave added support to the diagnosis.

In 7 of the 20 patients with elevated I^{131} uptake there were either typical signs and symptoms or findings in the thyroid gland that prompted the suspicion of hyperthyroidism. In 13 patients the absence of signs and symptoms, and the lack of palpable abnormalities of the thyroid, had suggested a normal thyroid status and led to the diagnosis of primary cardiac disease.

The BMR is an unreliable criterion of thyroid function in the presence of heart disease, because of the undue elevation of the BMR which occurs in patients with cardiac insufficiency and the relatively slight elevation in the BMR noted in patients with mild hyperthyroidism. The level of serum cholesterol bore no relation to the degree of thyroid function.

I^{131} uptake studies are of value in revealing otherwise undetected hypermetabolism which may cause or aggravate organic heart disease.

The Disposal of I^{131} -Labeled Thyroxine in Myxedema, Euthyroidism and Artificial Hyperthyroidism. Philip C. Johnson* and William H. Beierwaltes, Ann Arbor.

Five adults were given less than 0.1 mg. of Na- I -thyroxine, orally, labeled with 585-924 microcuries of I^{131} . The experimental subjects were a patient with classic myxedema following total thyroidectomy, with artificial hyperthyroidism induced by desiccated thyroid given to 15 grains per day; 2 euthyroids with biliary fistulae; 1 untreated primary myxedema; and 1 intact euthyroid. Quantitative I^{131} analyses were made on urine and bile specimens every hour for 6 hours, then on 24-hour specimens for 6 days. Quantitative total fecal I^{131} analyses were made daily for 6 days. Quantitative inorganic and "thyroxine" I^{131} chromatography was performed on daily 24-hour urine specimens for 3 days in the control euthyroid patient.

The most striking findings were: (1) total 6-day I^{131} excretion in urine and stool was similar in magnitude in these myxedematous, euthyroid and hyperthyroid subjects; (2) the enterohepatic circulation of thyroxine-derived I^{131} was found to be much less than in animals; (3) the fecal excretion of thyroxine-derived I^{131} was the same both in bile fistula and in intact patients. These findings indicate that thyroxine is present in the feces not because of fecal bile, but either through lack of absorption from gut or active excretion through gut wall. The fact that

metabolism of intravenous thyroxine and oral thyroxine is reportedly the same would suggest that the latter explanation is more probable.

A Radiiodine (I^{131}) Tracer Study of the Survival of Thyroid Autotransplants in Man. D. Emerick Szilagyi, John L. Barrett* and Nicholas P. D. Smyth*, Department of Surgery, Henry Ford Hospital, Detroit.

During the past 2 years, in a group of 9 patients with Graves' disease and with toxic and nontoxic adenomatous goiter, the physiologic activity of thyroid autotransplants was studied after thyroidectomies of varying radicality. At intervals of 12 to 24 weeks, the functional state of the transplants (of graded size and placed in the sternocleidomastoid muscle) was evaluated by determining the uptake of radioiodine, while the level of total thyroid function was measured in terms of radioiodine total uptake and excretion, basal metabolic rate and the cholesterol and protein-bound iodine content of the blood. All transplants survived and showed endocrine activity. The degree of this activity appeared to depend on the length of survival, the degree of hyperplasia of the transplanted tissue and the systemic demand for thyroxine production. In some instances, in which—as judged by other experiments—the amount of thyroid tissue left in situ at operation would have led to hypothyroidism, the functional capacity of the transplants was sufficient to maintain the patient in a euthyroid state. Some clinical aspects of these findings having to do with recurrent hyperthyroidism and postoperative hypothyroidism will be briefly discussed.

Functional Changes in the Thyroid Remnant after Subtotal Thyroidectomy. D. Emerick Szilagyi, Nicholas P. D. Smyth,* John L. Barrett* and Edward E. Longabaugh,* Department of Surgery, Henry Ford Hospital, Detroit.

During the past two and one-half years, two factors of importance in the genesis of postoperative persistent and recurrent thyrotoxicosis—the size and the growth potentiality of the thyroid parenchyma left in situ at operation—have been studied in 28 cases of subtotal thyroidectomy performed for toxic and nontoxic adenomatous (17 cases) and for diffuse hyperplastic goiter (11 cases).

The radicalness of the operation was controlled by careful measurement of the tissue remnants (weighing from 0.050 to 3.5 Gm.), by a "matched-weight" method. The functional capacity of the remaining thyroid parenchyma was estimated by I^{131} uptake and excretion studied. Thus the interrelationship between the size and postoperative age of the tissue remnant on the one hand and the changes in its functional capacity (i.e., its avidity for iodine) on the other have been followed serially and compared with the clinical course and such other laboratory indices of thyroid activity as basal

metabolic rate and the level of blood protein-bound iodine and cholesterol.

The thyroid tissue remnant showed some measure of functional growth (regeneration?) in every instance, the degree being in fair correlation with the degree of hyperplasia and level of functional activity of the gland before operation. The minimal amount of thyroid tissue to be spared for the maintenance of euthyroidism was found to be much less than hitherto assumed; in cases of moderate thyrotoxicosis 0.8-1.0 Gm., in those of severe thyrotoxicosis, 0.5 Gm. of thyroid parenchyma usually seemed adequate. The clinical implications of these observations will be briefly discussed.

X-Ray Treatment of Malignant Exophthalmos: A Report on 28 Patients. *William H. Beierwaltes, Ann Arbor.*

The method of selection, treatment, and follow-up of 10 patients with "malignant exophthalmos" treated by irradiation of the pituitary has been published by the author (*J. Clin. Endocrinol.* 11: 512, 1951). Review of data on 18 more of our patients so treated and follow-up of the previously treated patients suggest methods of selection that will insure a higher percentage of good results.

Thirteen of the total of 28 patients showed a significant response in exophthalmometer measurements after this treatment. Eleven of these 13 patients, in retrospect, began to show response in less than 7 months after x-ray, but this response was usually not apparent within the first month after x-ray therapy. Maximum recession of the eyes reached a median of about 3-4 mm. during the 19-month average follow-up after irradiation, with maximum recession of 15 mm. in one patient and 10 mm. in another. Generally, other signs of malignant exophthalmos improved when the exophthalmos receded significantly. Our data suggest that malignant exophthalmos usually responds to x-irradiation of this type if the exophthalmos has been present less than one year and rarely responds if it has been present more than two years. Patients with coexistent thyrotoxicosis and malignant exophthalmos had exophthalmos more resistant to treatment than patients without active thyrotoxicosis. No difference in response of exophthalmos was found after x-ray therapy between the group of patients fed desiccated thyroid up through the time of x-ray therapy and patients not fed thyroid.

The Creatine Metabolic Defect in a Case of Concurrent Hyperthyroidism and Myasthenia Gravis. *Richmond W. Smith, Jr., Robert Berghan* and Clarke A. McColl,* Divisions of Endocrinology and General Medicine, Henry Ford Hospital, Detroit.*

The creatine metabolic defect has been studied in a 54 year old female with concurrent hyperthyroidism (BMR plus 40%) and myasthenia

gravis. Moderately advanced muscle wasting characteristic of thyrotoxic myopathy was present, while the muscle weakness responded impressively to prostigmine. The creatine coefficient was 13. Predicted hypercreatinuria was not present. In fact, spontaneous creatine excretion was negligible and the creatine tolerance test revealed a retention approaching 100%. Analysis of biopsied muscle indicated significant depletion of creatine content. This over-all unusual metabolic derangement could be explained by the presence of hepatic damage. Such was found to be the case. Dietary measures, iodine and 6-propylthiouracil led to general improvement and control of the hyperthyroidism. Concomitantly, a paradoxical hypercreatinuria appeared which, as the BMR fell, progressively increased and was associated with a reversal of creatine tolerance. The creatine coefficient rose to 18. During this period the myasthenia gravis worsened with a 3-fold increase in prostigmine requirements. ACTH appeared to augment the hypercreatinuria but induced a marked improvement in the myasthenia gravis 3 days after the hormone had been discontinued.

These studies demonstrate that hypercreatinuria is not an obligatory chemical derangement of known active myopathic disease. Indeed, creatine may be avidly retained. The presence of severe functional liver disease was the determining factor in this case. It emphasizes that the validity of spontaneous creatine excretion and creatine tolerance studies as measures of the rate of muscle breakdown, depends on the normal rate of creatine elaboration by the liver.

Evaluation of Parathyroid Function by a Calcium Infusion Technic. *Lawrence H. Kyle, Marcus Schaaf* and Leonard A. Erdman,* Department of Medicine, Georgetown University School of Medicine and the Georgetown University Hospital, Washington, D. C.*

This study concerns the mineral alterations which result from the infusion of calcium to patients with and without parathyroid disease. Blood and urinary calcium and phosphorus were measured before, during and after the intravenous administration of calcium, constant mineral intake being maintained during the entire test.

A fairly constant pattern of change was noted in the control subjects. Accompanying the rise in serum calcium there was significant elevation of serum phosphorus. Although a moderate decrease in urinary phosphorus excretion usually occurred during the infusion, this was neither constant nor of sufficient degree to account for the hyperphosphatemia. All control subjects demonstrated a decrease in the 24-hour urinary phosphate excretion on the day of infusion. In 2 patients with hypoparathyroidism, infusion of calcium was accompanied by an increase in phosphate excretion and a slight fall in

serum phosphorus. In hyperparathyroidism due to tumor there was neither rise in serum phosphorus nor significant decrease in urinary phosphate excretion. These findings would suggest that elevation of blood calcium suppresses activity of normal parathyroid tissue with consequent hyperphosphatemia and decrease in urinary phosphorus. However, the addition of parathyroid extract to the infusate prevented the rise in serum phosphorus without

causing significant alteration of the usual decrease in urinary phosphorus. The results of this investigation indicate that parathyroid hormone affects blood phosphorus by extrarenal mechanisms, and suggest that changes in urinary phosphate are not directly related to the action of parathyroid hormone. The calcium infusion technic appears to be of value in the study of parathyroid physiology and useful in the diagnosis of parathyroid disorders.

EPIDEMIOLOGY AND PUBLIC HEALTH

The "Host Factor" in Human Illness: The Occurrence of Major Differences in Susceptibility to Illness among a Group of Adult Women. *Lawrence E. Hinkle, Jr., and Norman Plummer,** Department of Medicine, New York Hospital-Cornell Medical Center, New York.

A study was made of all of the illnesses which had occurred in 1297 telephone operators in New York City, a group essentially homogeneous in age, sex, area of domicile, place and type of work, economic, social and cultural background. None had shown evidence of significant illness when employed in adolescence, and a record was available of every subsequent illness of each woman for up to 35 years thereafter.

Of the episodes of illness, 69% had occurred in only 37.8% of the women, and the same women fell into the high and low illness groups year after year. Twenty frequently ill women, 20 well women, and others in intermediate groups, selected at random, were examined and interviewed at length. The average ill woman had had 62.05 minor and 10.1 major episodes of illness, 4.55 minor and 2.35 major accidents, 2.5 surgical operations, and 1210 days of disability during 25.9 years; whereas the average well woman had had 6.1 minor, and 0.65 major episodes of illness, 1.6 minor and 0.3 major accidents, 0.25 surgical operations, and 33.3 days of disability during 28.8 years. Each frequently ill woman had had illnesses in several organ systems, as well as generalized infections, metabolic disturbances, tumors, psychological disorders, and accidents.

The evidence indicates that some of these women had a high incidence of all forms of illness, while others had few illnesses of any form. These differences in total amount of illness could not be accounted for by malingering, psychological disturbances, heredity, economic background, nutrition, or exposure to infection. In contrast to the well women, ill women had been exposed to stressful life situations much of the time throughout adult life. The alteration in bodily function which accompanied their attempts to adapt to these situations appeared to be the most important factor in their susceptibility to disease.

The Role of Contaminated Environment in the Transmission of Group A Streptococci. *William D. Perry, Lewis W. Wannamaker and Alan C. Siegel,* Streptococcal Disease Laboratory and the Medical Service, USAF Hospital, Warren Air Force Base, Wyoming, and the Department of Preventive Medicine, Western Reserve University, Cleveland. (This investigation was conducted under the sponsorship of the Commission on Acute Respiratory Diseases and the Commission on Streptococcal Diseases, Armed Forces Epidemiological Board, and was supported by the Offices of the Surgeons General, Departments of the Army and Air Force, Washington, D. C.)

The development of effective measures for the control of the transmission of streptococcal infections has been handicapped by lack of definitive information on relative role of human reservoirs and contaminated environment. This study is concerned with the importance of the environmental reservoir.

Blankets naturally contaminated with group A streptococci were issued to men with negative throat cultures. Another group of men received freshly laundered blankets. No significant difference in incidence of streptococcal disease was observed in the two groups.

Dust containing large numbers of group A hemolytic streptococci was collected at intervals from barracks where the streptococcal disease rates were high. The dust was then introduced into a barrack where there were no streptococcal carriers. No increase in streptococcal disease was observed in this barrack as compared to control groups.

The failure to produce disease with naturally contaminated blankets and dust suggested that the streptococci, although viable, were not infectious. Introduction of such dust directly into the oropharynx of volunteers has thus far not resulted in infection. These studies indicate that contaminated environment probably plays a minor role in the spread of streptococcal disease.

A Water-borne Outbreak of Canicola Fever. *Hugh R. Williams,* Martha K. Ward,* J. E. McCroan* and L. E. Starr* (introduced by Alexander D.

Langmuir), Georgia Department of Public Health and the Communicable Disease Center, U. S. Public Health Service, Federal Security Agency, Atlanta. (The authors wish to thank W. D. Murphy, Director, Division of Epidemiology, Georgia State Health Department, for his very real assistance in the conduct of this study.)

During July, 1952, 26 cases of *Leptospira canicola* infection occurred among 141 persons in a rural settlement near Columbus, Georgia. The illness was characterized by abrupt onset of chills, fever, headache, severe myalgia, and arthralgia. Many also had nausea, vomiting, with or without diarrhea, conjunctival injection and stiffness of the neck. Frank jaundice was absent. *L. canicola* was isolated by culture from blood of one case on the 10th day, and from urine of another by hamster passage on

the 35th day. All 26 cases were confirmed serologically by agglutination or complement-fixation tests.

All patients had been swimming in a water hole fed by a small sluggish creek. The attack rate among those who had any contact with the creek water was 47%. The illness rate varied directly with frequency of swimming and extent and vigor of immersion. Serologic study of animals having access to the creek above the swimming hole before and during the epidemic showed that 14 of 22 settlement dogs, all of 3 farm swine, and 2 of 21 cattle had been infected with *L. canicola*. Three of 8 positive dogs, and 1 of the 3 swine yielded *L. canicola* on hamster inoculation of urine. This is thought to be the first known naturally occurring *L. canicola* infection in swine and cattle as well as the first recorded outbreak of water-borne canicola fever in man.

GASTROINTESTINAL SYSTEM

A Quantitative Study of the Phases of Gastric Secretion in a Human Subject. Henry D. Janowitz, Franklin Hollander* and Asher Winkelstein,* Gastroenterology Research Laboratory, The Mount Sinai Hospital, New York.

To obtain information on the magnitude of the phases of gastric secretion, studies were conducted on a female adult with esophageal stenosis and a gastric fistula. The volume of secretion and its content of HCl and pepsin were determined during the cephalic, gastric, intestinal, and interdigestive phases.

The cephalic phase persisted for several hours after sham feeding of a meal selected by the subject (means for 12 experiments: volume, 212 ml.; HCl, 16 mEq.; pepsin, 53,000 Hgb. units), and exceeded that provoked by insulin hypoglycemia (volume, 113 ml.; HCl, 12 mEq.; pepsin, 48,000 units) or histamine (volume, 80 ml.; HCl, 5 mEq.; pepsin, 8,900 units). The gastric phase was smaller, whether elicited by antral distention with 200 ml. air (means of 10 experiments: volume, 33.5 ml.; HCl, 1.4 mEq.; pepsin, 6,200 units), or protein secretagogues (means of 3 experiments with 7.5 Gm. of liver powder: volume, 20.2 ml.; HCl, 1.2 mEq.; pepsin, 4,200 units). Of 7 amino acids, only β -alanine evoked a response (mean of 5 experiments: volume, 25.1 ml.; HCl, 2.2 mEq.; pepsin, 1,280 units). The intestinal phase, following intraduodenal instillation of a variety of protein secretagogues was of minor importance. The unstimulated interdigestive phase contributed significantly to the total secretion (hourly means for 12 experiments: volume, 33 ml.; HCl, 1.3 mEq.; pepsin, 4,060 units).

The Comparative Effects of Various Anticholinergic Agents on Human Gastric Acid Secretion. John McGowan,* Malcolm M. Stanley and John Powell,*

Pratt Diagnostic Clinic-New England Center Hospital, Boston.

The effects on gastric acid secretion of single oral or parenteral doses of 11 drugs were studied in 110 patients, including 45 with peptic ulcers studied by basal secretion and double meal technics. An additional 26 controls included 12 with peptic ulcers. The possibility of cumulative effects was not investigated.

There was considerable variation in response from patient to patient to similar doses of the same drugs. Achlorhydria following oral administration occurred rarely, and only after large doses of more potent agents. The correlation between effects on acid secretion and dryness of mouth and blurring of vision was striking. No drug effectively inhibited secretion without these "side effects." With currently available drugs, patients must accept xerostomia if adequate acid inhibition is to be obtained.

The following approximate single oral doses of drugs will reduce fasting secretion in patients with ulcers, or food-stimulated secretion in normals, by 20-50% or more for 2-4 hours: Atropine, 1.3 mg.; Antrenyl, 10-25 mg.; Ro 2-3773 (Hoffman-LaRoche), 10-35 mg.; Probanthine, 30-60 mg.; 2963 (Squibb), 75-125 mg.; Banthine and 3199 (Squibb), 100-150 mg.; Prantal, 3505, 2998 and 2806 (Squibb), 400-700 mg.

Smaller parenteral doses of most of the above produce achlorhydria more frequently suggesting that some of the observed differences are due to inequalities in absorption or transport of orally administered medication.

The Suppressing Effect of Banthine on Gastric and External Pancreatic Secretion in Man. R. M. Whitrock, R. W. Hansen,* R. L. Finch and M. B.

Chenoweth, Departments of Pharmacology and Surgery, University of Michigan, Ann Arbor.

A controlled study was undertaken to establish the effect of low oral doses of Banthine on gastric and external pancreatic secretions. The gastric and pancreatic secretions were collected separately through a three lumen tube with an inflatable balloon effectively obstructing the pylorus. Eight normal young men passed the tube orally for 22 control and 16 test collections. The tube position was verified by fluoroscopy. A two-day rest period elapsed between each test. The men were tested in the fasting state.

In the control series, the resting gastric and duodenal contents were aspirated for 20 minutes. A stimulus of urocholine 4 mg. and histamine 0.3 mg. was injected subcutaneously. Aspirations were collected in 20 minute samples for a total of 80 minutes.

With the test series, resting secretions were again collected for 20 minutes. Fifty mg. of Banthine dissolved in 10 cc. of distilled water was introduced directly into the duodenum through the tube. A 30 minute period was allowed for drug absorption. The duodenal and gastric contents were aspirated for 10 minutes and discarded. The test procedure then duplicated the control series.

Laboratory tests were carried out immediately as the collections became available. Gastric collections were assayed for volume, free and combined HCl and pepsin. Duodenal collections were assayed for volume, HCO₃ and amylase.

Results: 1. Banthine suppressed gastric volume about 60% without changing acid or pepsin concentration. 2. Banthine completely suppressed pancreatic secretion.

Observations on Small Intestinal Function in Patients with Ileostomies. *Alvin J. Cummins*, The Gastro-Intestinal Section, Kinsey-Thomas Foundation of the Medical Clinic, Hospital of the University of Pennsylvania, Philadelphia.

Observations were made on ileal function in five patients with ileostomies by means of balloon-kymographic motility studies and direct measurements of the fragility and blood flow of the exposed mucosa, as reflected in mucosal color. Emotionally stressful interviews produced hypermotility of the intestine and increased fragility and blood flow of the mucosa, in each case. The ingestion of food, or in some cases the mere anticipation of eating resulted in similar ileal hyperfunction. The jejunum also participates in the hypermotility response to eating, as demonstrated by oral intubation studies in two normal patients with intact gastro-intestinal tracts. Clinically used oral doses of anticholinergic drugs failed to block these responses but large intravenous doses abolished entirely the "gastro-ileal" reflex.

These studies are interpreted as demonstrating

the participation of the small intestine in the responses to emotional stress previously documented for the human stomach and colon, and may thus aid our understanding of the functional derangements of the bowel. In addition, they help to elucidate the mechanisms involved in production of the "gastro-ileal" reflex, and may explain the increased absorption rate which may occur during intestinal hypermotility, through the demonstration of accompanying increased vascularity.

The Effect of Detergent on Intestinal Digestion. *Bertram Fuchs*,* (introduced by *John T. Farrar*), Boston.

Detergents are widely used for washing eating utensils and also have been used in the treatment of peptic ulcer. Since detergents are known to be enzymatic inhibitors, the effect of a typical anionic detergent, sodium lauryl sulfate (SLS), on intestinal digestion and absorption has been studied. In vitro tests, using duodenal drainage fluid obtained after secretin stimulation, showed that SLS produces a marked inhibition of pancreatic amylase, lipase and trypsin.

To determine the in vivo effect of SLS on the digestion and absorption of starch, lipid and protein, tolerance tests measuring blood levels of the products of digestion were analyzed. To eliminate the effect of different gastric emptying rates, all test materials were instilled directly into the duodenum through a Levine tube. Each subject served as his own control and was studied with and without detergent added to the test substance. Carbohydrate, in the form of boiled rice, was given, and the blood glucose levels were measured. Natural vitamin A ester was used as the test substance for lipid. Blood levels of glycine following administration of gelatine served as an index of protein digestion.

In most tests, 2 Gm. of SLS lowered the blood levels of glucose, vitamin A and glycine, as determined after the administration of the test substances. In the treatment of peptic ulcer, others have used up to 10 Gm. of detergent a day.

Combined Serum and Duodenal Amylase Study in Pancreatic Insufficiency. *James Otey Burke, Kemp Plummer, Benjamin B. Weisinger, III** and *Sarah Bradford**, V. A. Hospital, Richmond, and Department of Medicine, Medical College of Virginia.

A combined and simultaneous study of the serum amylase and duodenal bicarbonate and amylase content following secretin administration in eleven patients with chronic pancreatic disease reveals an apparent correlation. The serum values remain quite low while the duodenal values indicate pancreatic insufficiency. It is suggested that low serum amylase values are as significant as high values in the diagnosis of interval pancreatic inflammation and carcinoma.

INFECTIOUS DISEASES—ANTIBIOTICS

Persistence of *Rickettsia rickettsii* in a Patient Recovered from Rocky Mountain Spotted Fever. R. T. Parker,* P. O. Menon, A. M. Merideth, M. J. Snyder, and T. E. Woodward, Section of Infectious Diseases, University of Maryland School of Medicine (introduced by Philip Y. Patterson).

The etiologic agents of epidemic, murine and scrub typhus have been shown to persist in the tissues of experimental animals for considerable periods of time. However, after recovery from experimental infections, the rickettsiae of Rocky Mountain spotted fever have been isolated for only a short interval. In human beings, there is evidence that rickettsiae remain dormant but viable following scrub typhus.

In this study, attempts were made to isolate *Rickettsia rickettsii* from the tissue of a patient who had recovered from Rocky Mountain spotted fever following antibiotic therapy. An inguinal lymph gland was excised one year after a severe attack of this disease. The node, after storage at -70°C . for 29 months, was emulsified and inoculated intraperitoneally into guinea pigs previously given cortisone acetate. These animals showed a febrile response. The recovered agent was maintained by serial passage through guinea pigs. Subsequently, specific complement fixing antibodies for Rocky Mountain spotted fever were demonstrated in the sera of these animals and pathologic lesions of this disease were found. Moreover, the isolated agent was capable of infecting fertile hens' eggs; and intracellular organisms morphologically and tinctorially identical with *R. rickettsii* were observed repeatedly.

Therefore, viable organisms have been isolated from the lymphatic tissue of a patient who had remained asymptomatic for one year after an active rickettsial infection. This evidence provides additional confirmation of the "immunity of tolerance" concept which Zinsser hypothesized to explain the pathogenesis of Brill's disease. In addition, this observation suggests the possibility that a recrudescent form of Rocky Mountain spotted fever may occur.

Platelet Agglutination by Influenza Virus. Arno G. Motulsky* (introduced by Milton H. Paul), Department of Hematology, Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington, D. C.

Pure, smooth and stable human and rabbit platelet suspensions were prepared using silicone glassware, sequestrene as an anticoagulant and differential centrifugation with refrigerated centrifuge. Suspensions of influenza virus in chorioallantoic fluid were placed into test tubes containing washed platelet suspensions in sequestrene. The

tubes were observed for agglutination grossly and microscopically after storage at 4°C . for 15 hours. Influenza virus (PR 8, Lee and FM 1) in dilutions up to 1:4 produced definite agglutination of platelet suspensions. Chorioallantoic fluid controls were negative. Specific influenza anti-sera in dilutions up to 1:40 inhibited this agglutination while normal sera failed to do so. Elution could not be demonstrated since the supernatant of the virus platelet preparations did not agglutinate new platelet suspensions. Red cell agglutination in low titer, however, still occurred with the supernatant.

These observations and the recent demonstration of agglutination of tissue culture fibroblasts by viruses illustrate the ability of viruses to attach to the surface of a variety of "cells". In view of findings that virus-modified red cells may act as autoantigens in the production of autoimmune acquired hemolytic anemia, the demonstration of platelet agglutinins by a virus suggests that virus modified platelets may play a similar role in the production of platelet agglutinins in some cases of thrombocytopenia.

Effect of Proteolytic Enzymes on Respiratory Secretions of Patients with Acute Poliomyelitis. Sidney Kofman*, Mark H. Lepper, George Gee Jackson and Harry F. Dowling, University of Illinois College of Medicine, Chicago.

Atelectasis is one of the main complications of patients with poliomyelitis who have tracheotomies and are in respirators. Proteolytic enzymes have been recommended to reduce the viscosity of tracheal secretions and thus aid in their aspiration. In the present studies, patients received one of the following aerosol solutions: 250,000 units of trypsin in 6 cc. of phosphate buffer, or streptokinase (100,000 units) and streptodornase (25,000 units) in 6 cc. of isotonic sodium chloride, or 6 cc. of isotonic sodium chloride solution as a control. Laboratory tests on the tracheal secretions included determination of viscosity, volume, % sediment, total and % sediment nitrogen, pH and reducing substances. Trypsin decreased the viscosity of tracheal secretions without affecting the % sediment or total nitrogen. The streptococcal enzymes decreased the viscosity, % sediment, and total nitrogen and increased the volume.

Twenty-four patients received either aerosol antibiotics and proteolytic enzymes, or antibiotics and sodium chloride as prophylaxis against pulmonary complications. There were no apparent differences in any of the groups. Three patients exhibited toxic reactions with the streptococcal enzymes and in one of these patients pneumonia occurred. Twelve patients received 21 instillations of trypsin directly into a main stem bronchus, and

9 patients received 10 direct instillations of isotonic sodium chloride. Adverse and beneficial effects will be discussed.

Studies on the Complement-Fixing Antigen of Herpes Simplex. *Charles V. Adair*, Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington, D. C.

Embryonated eggs infected by the yolk sac route with any of three strains of herpes simplex virus provided complement-fixing antigen in the allantoic and amniotic fluids. Ultracentrifugation studies on allantoic fluid from eggs infected with the Z strain showed that a soluble antigen, separable from the infectious virus particle, provided the main complement-fixing activity of such materials.

Complement-fixation tests employing this soluble antigen and sera from normal persons in various age groups showed that almost half of the adult population possesses such antibodies in titers of 1:4 to 1:32 with a mode at 1:16. Ten patients with recurrent herpes labialis displayed antibody titers of 1:8 to 1:32. Attempts to isolate the virus were made on 7 of these ten and yielded the agent in 5 instances. Only 2 of the 10 with recurrent herpes developed significant increases in complement-fixing antibodies during convalescence. Only 2 of the 4 cases of primary herpes infection, confirmed, by both isolation and serum neutralization data developed complement-fixing antibodies.

An evaluation of the relative usefulness of the egg membrane neutralization and complement-fixation techniques in the diagnosis of herpes simplex infections suggests generally that the latter alone may be sufficient for such purposes.

Nitrogen Balance in Hepatitis. *Irvin C. Plough** and *Victor M. Sborov*, Department of Hepatic and Metabolic Diseases, Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington, D. C.

Among the manifestations of acute viral hepatitis are gastrointestinal disturbances and changes in serum proteins. It is to be anticipated that these changes would be accompanied by abnormalities in the handling of ingested protein. To evaluate such changes nitrogen balance studies were made in three patients with early acute viral hepatitis beginning on the third day of jaundice. A constant intake of 60 Gm. of protein and 2000 calories per day was maintained for a 3-week period. Nitrogen balance was correlated with the balances of potassium, phosphorus, sodium, and water, and with serum proteins, tests of liver function, body weight and creatinine excretion. Two of these patients were wounded soldiers who developed hepatitis 83 and 104 days after receiving blood and plasma transfusions. The third patient was believed to have epidemic hepatitis.

The average daily nitrogen balance in the first

two patients was -0.52 and -0.37 Gm. per day respectively. There was no definite trend in the nitrogen balance in these two patients. The third patient showed an average daily balance of -1.48 Gm. There was a gradual decrease in the negative balance to almost zero at the end of the 3-week period. No clear correlation with improvement in liver function could be seen among the other balances measured.

These studies suggest that the degree of initial depletion of the protein stores of the entire body more strongly governs nitrogen balance than does the change in liver function associated with hepatitis.

The Effects of Strenuous Exercise on Patients Convalescent from Acute Infectious Hepatitis.

Richard D. Eckhardt, Thomas C. Chalmers, William E. Reynolds, Robert W. Reifstein, Norman Deane*, Clifford W. Smith*, Hunter A. Soper*, Joaquin G. Cigarroa*, and Charles S. Davidson*, Thorndike Memorial Laboratory, Boston City Hospital and Harvard Medical School, Boston.

The effects of strenuous exercise early in the convalescent phase of infectious hepatitis were studied in 180 Army patients hospitalized in Japan. During their acute phase the subjects were given varying diets and allowed out of bed at will. One half the patients, randomly selected on admission, began a 2-week rehabilitation program an average of 3.3 days after their total serum bilirubin reached 1.5 mg.% and their bromsulfalein retention 5%. The other half were kept in the hospital for an average of 11.6 days (Period I) and then exercised for one week (Period II). Rehabilitation consisted of calisthenics, athletics and 5- to 9-mile marches over rough terrain. Both groups were followed by twice-weekly clinical and laboratory observations.

Minor fluctuations in symptoms and signs occurred in both groups. No patients developed recurrent jaundice, but 5% of each group had asymptomatic bromsulfalein relapses. Mean total serum bilirubin trend curves of the early exercise group revealed a significant rise during Period I followed by a steady fall towards normal as exercise continued. The control group bilirubin curve continued to fall during Period I and rose to a level slightly above the early group at the end of Period II. The one-minute bilirubin, thymol and zinc turbidity tests were unaffected by exercise. A follow-up study now under way has as yet revealed no significant differences between the two groups.

Conclusion: Strenuous exercise early in convalescence from hepatitis results in minor changes of doubtful clinical significance.

The Relationship of Stress, Adrenocortical Function and Tuberculosis. *Thomas H. Holmes, Edmund R. Clarke* and Daniel Zahn*. The Departments of

Physiology and Biophysics and of Psychiatry of the University of Washington School of Medicine, and Firland Sanatorium, Seattle. (Supported in part by a contract between the University of Washington and the Alaskan Air Command, Arctic Aeromedical Laboratory, Ladd Air Force Base, Fairbanks).

The mechanisms whereby life stress may influence the natural history of tuberculosis have been investigated. The urinary excretion of 17-ketosteroids, utilized as an index of adrenocortical function, has been studied and correlated with patterns of behavior, emotional reactions and pulmonary tuberculosis in 75 patients.

The mean 17-ketosteroid value in 20 females (43 determinations) was 8.78 mg./24 hrs. with a range of 2.38 to 24.70 mg./24 hrs. In 71 males (160 determinations) the mean was 8.81 mg./24 hrs. with a range of 1.78 to 38.42 mg./24 hrs. A striking correlation was found to exist between the character of the tuberculous lesion in the lungs, the behavior patterns of the patients, and the excretion of 17-ketosteroids. Fibrotic disease, usually limited in extent, was characteristically found in tense, anxious, restless patients who were neither acutely ill nor febrile but whose interpersonal and social adjustments were conflict-ridden. In these patients the 17-ketosteroid levels were 20 mg./24 hrs. or over. Conversely, exudative disease, usually of considerable extent, characteristically occurred in acutely ill, febrile patients who were also withdrawn, apathetic or depressed. In these patients the excretion of 17-ketosteroids was 2 mg./24 hrs. or less. The difference in the 17-ketosteroid values for these two categories of patients was statistically significant. Those patients who manifested superficial calm and acceptance of the hospital setting had excretion values ranging from 10 to 15 mg./24 hrs. and exhibited predominantly fibrotic disease, which tended to be stable. The behavior of the "chronic custodial" patients manifested both anxiety and depressive features, and was associated with 17-ketosteroid values ranging from 4 to 10 mg./24 hrs. and predominantly exudative disease which tended to be unstable.

Conclusion: Adrenocortical hormones play an important role in the mechanisms of resistance in tuberculosis; and life stress, by engendering alterations in adrenocortical function, may influence resistance to the disease.

The Combination of ACTH and Cortisone with Antibiotic Therapy in the Management of Overwhelmingly Severe Infections. Theory and Practice Based on More Than Two Years Experience. J. P. Jahn*, L. Boling, T. R. Meagher*, H. H. Peterson*, B. M. Fisher*, A. E. Thill* and L. W. Kinsell, Institute for Metabolic Research and the Departments of Surgery, Medicine, and Pediat-

rics, Highland-Alameda County Hospital, Oakland.

Corticotrophin, cortisone, hydrocortisone and related compounds significantly modify the inflammatory reaction. As part of this effect, or in some other manner, they diminish or eliminate the systemic toxicity in patients suffering from a variety of severe specific infections, without in any way inhibiting the growth of the infectious agent. They also exert a major "anti-shock" effect by way of improvement in the total circulatory status.

Because of the preceding it seemed advisable to evaluate the effects of these agents in conjunction with intensive antibiotic therapy in patients suffering from specific infections with known antibiotic sensitivity, but in whom, because of late institution of treatment, or poor resistance on the part of the patient, showed an inadequate response to antibiotic therapy. During the past two years, such combined treatment has been used in patients suffering from a variety of infections including meningococcemia, pneumococcal meningitis and widespread peritonitis. Many of these patients were considered moribund on admission to the infectious disease and surgical services of the County Hospital. More than 68 such patients have been treated up to the present time. On the basis of this experience it appears unequivocally established that such combined therapy results in impressive reduction in morbidity and mortality. Because of the diminished tendency to localization of infection, certain hazards are attendant upon such combined therapy. These hazards can be minimized or eliminated in most instances. Methods and data will be presented and discussed.

Adrenal Cortical Function During Isonicotinic Acid Hydrazide Therapy. Thomas F. Frawley, Reuben J. Erickson* and Paul J. Rosch, Albany Medical College and Albany Hospital, Albany.

In a group of 8 patients with active pulmonary tuberculosis adrenal cortical function has been studied during isonicotinic acid hydrazide (INH) therapy. An 8-hour intravenous ACTH test (20 I.U.) was performed at bi-monthly intervals and measurements were made of the urinary 17-ketosteroids, 17-hydroxysteroids, uric acid-creatinine ratio, and percentage fall in circulating eosinophils. There were no significant changes in the average fasting eosinophil level over a 3 to 6-month period. The eosinopenic response to ACTH averaged 80% before treatment and 85% following institution of INH therapy (5 mg./Kg. body weight). A spontaneous increase in 17-ketosteroid excretion ranging from 4 to 7 mg. per 24 hours was observed in both males and females after 4 to 6 weeks. All patients showed evidence of an enhanced 17-ketosteroid excretion response to ACTH ranging from 24% to 33% above the initial ACTH response. This lasted 8 to 12 weeks. The uric acid-creatinine ratio and 17-

ketosteroid excretion showed no appreciable change throughout the period of study. No evidence was obtained that INH causes any significant change in corticosteroid (S-Hormone) production. Therefore, an increased production of this fraction of the adrenal steroids does not explain the sense of well-being and increased appetite and muscle strength observed in patients treated with niazide derivatives. The functional alteration in the pituitary-adrenal system manifested by the temporary increase in adrenal cortical production of 17-ketosteroids (N-Hormone) is considered a secondary rather than a primary effect of INH administration.

The Intravenous Use of A Combination of Sodium Para-Aminosalicylate and Polyvinyl Pyrrolidone in the Chemotherapy of Tuberculosis. *William Weiss, Marvin Seven* and George M. Eisenberg, Philadelphia General Hospital, Philadelphia.*

French investigators have reported that 3.5% Polyvinyl Pyrrolidone can be used as a vehicle for various drugs with the purpose of retarding absorption and excretion. In this way, smaller doses of sodium PAS may be given intravenously with resulting high concentrations of PAS in the blood over a longer period of time. In this study the intravenous use of a preparation of 25% sodium PAS in 3.5% PVP has been compared with the intravenous use of 25% sodium PAS alone. It has been shown that PVP does not interfere with the bacteriostatic efficacy of PAS against tubercle bacilli in vitro. PVP acts to maintain higher and more prolonged blood levels of PAS and it does not prevent PAS from passing into the cerebrospinal fluid in adequate amounts. PAS-PVP has been used therapeutically for periods up to four weeks without significant toxicity. This preparation has the advantage that it can be given by syringe injection; and smaller amounts of PAS are needed to establish high concentrations of PAS in the blood and spinal fluid.

The Use of Isoniazid and Streptomycin Plus Isoniazid in the Management of Acute Tuberculous Pneumonia; Including Laboratory Studies. *Sol Katz*, George McCormick*, Patrick Storey*, Monroe J. Romansky and Edward Marshall*, (introduced by Monroe Romansky), Pulmonary Disease Division of Gallinger Municipal Hospital and Department of Medicine, George Washington School of Medicine and Georgetown Medical School, Washington (supported by a Grant from the Lasdon Foundation).*

We have had experience with the use of Isoniazid in over 200 patients with all forms of tuberculosis. This drug has been used alone, as well as in combination with other antituberculous agents. Because of striking success in the use of streptomycin twice weekly plus PAS daily in the management of patients with acute tuberculous pneumonia, it seemed desirable to evaluate the effect of inter-

mittent streptomycin plus daily Isoniazid in the treatment of this type of tuberculosis. Comparison was made with the results obtained with Isoniazid alone. The study included clinical, as well as laboratory observations. In vitro studies as set up contained 0.2 $\mu\text{g./ml.}$, 1.0 $\mu\text{g./ml.}$, 5 $\mu\text{g./ml.}$, 10 $\mu\text{g./ml.}$ of media. Gastrics or sputum specimens were collected before treatment and at 3- to 4-week intervals thereafter.

Twenty-two patients with acute tuberculous pneumonia received 1 Gm. of streptomycin twice a week plus 400 mg. of Isoniazid daily. All of the patients were severely ill, febrile and markedly toxic. Roentgenograms revealed extensive, confluent caseous-pneumonic or caseous-cavernous involvement. From 200 to 600 mg. of Isoniazid daily was administered to 15 additional patients with comparable disease. Neither group had received any prior therapy.

Striking therapeutic benefit, as judged from the effects on systemic manifestations, weight gain and appetite increase, were similar in both groups. X-ray improvement occurred sooner and was somewhat more marked in the patients receiving combination therapy. One patient receiving Isoniazid alone lost weight while another showed no significant x-ray improvement.

Emergence of tubercle bacilli resistant to one or more $\mu\text{g./ml.}$ of INH began at the third month in patients receiving INH alone. By the seventh month all cultures were resistant to one or more $\mu\text{g./ml.}$ in this group. In the patients who received combination therapy, resistance to one or more $\mu\text{g./ml.}$ of INH began in the fourth month and by the seventh month, two out of five positive cultures (40%) were resistant to one or more $\mu\text{g./ml.}$ Sputum conversion occurred in 86% of those receiving combination treatment compared to 50% in those receiving INH alone.

Erythromycin Laboratory and Clinical Studies in Over 75 Patients. *M. J. Romansky and R. E. Ritts, George Washington University, Medical Division, Washington, D. C.*

Since the advent of the antibiotics a changing pattern of bacterial sensitivity to these agents has occurred indicating a progressive development of resistance of certain microorganisms. Because of this there is a continuous need for new antibiotics. One of these, erythromycin, although having essentially the same bactericidal spectrum as penicillin, affects penicillin resistant bacteria; furthermore it is also effective against those gram-positive bacteria which are sensitive and resistant to the broad spectrum antibiotics and streptomycin. One of erythromycin's most important features is its activity against the hemolytic staphylococcus aureus. Adequate concentrations of erythromycin are obtained in the blood by the oral administration of 100 mg. or more at 4 hour intervals. Studies on the parenteral adminis-

tration of this agent will also be reported, as well as preliminary observations on the occurrence of cross resistance with other antibiotics.

The results of clinical trial in over 75 patients with pneumococcal pneumonia as well as other bacterial infections will be discussed; and tolerance of this antibiotic, following long term therapy, will be presented.

Studies on the Clinical Pharmacology of Carbomycin. *Henry Brainerd, Nobuyuki Kawata* and Mirra Scaparone**, Infectious Disease Laboratory, San Francisco Hospital and Department of Medicine, University of California School of Medicine, San Francisco.

The concentration of Carbomycin in serum and other body fluids was determined by a serial tube dilution method at various intervals following the administration of single doses of 2.0 Gm. orally or 0.5 Gm. intravenously to 38 subjects.

Unexpectedly low serum levels were observed in 15 nonjaundiced persons with normal liver function during 6 hours after administration. Peak concentrations occurred during the first 4 hours, followed by a sharp decline at 6 hours. Curves of serum concentration after oral and intravenous administration were similar. In 17 patients who had jaundice due to liver disease or extrahepatic biliary obstruction, variable but considerably higher serum concentrations than in "normals" were observed during the first 2 hours, and strikingly higher concentrations were obtained 4 and 6 hours after administration. The serum concentrations roughly paralleled the degree of icterus and did not depend on the level of serum albumin or state of kidney function. In 6 patients who had diffuse liver disease without jaundice, serum concentrations were variable but resembled those of nonjaundiced subjects.

Carbomycin appeared promptly in high concentration in the bile of 3 subjects. Urinary concentration of Carbomycin was very low in nonjaundiced persons, but was increased in the presence of jaundice. In all subjects only a small fraction of the administered dose was recovered in the urine during a 12-hour period. Carbomycin did not appear in the cerebrospinal fluid of 6 subjects within 6 hours of administration, regardless of serum concentration. In 2 jaundiced patients Carbomycin appeared in the ascitic fluid in high concentration.

It was concluded that low serum concentrations of Carbomycin were the result of rapid excretion in the bile.

The Effect of Aureomycin on Enzyme Systems of the Rat Liver. *Hyman J. Zimmerman and Fred L. Humoller**, Veterans Administration Hospital, Omaha.

The hepatic abnormalities said to follow aureomycin administration in humans and experimental animals are paradoxical in view of the reports of

beneficial effects from this antibiotic on patients with hepatic coma and animals fed diets producing hepatic necrosis. Likewise, the inhibition by aureomycin in vitro of respiration and oxidative phosphorylation of rat liver homogenates seems difficult to reconcile with the growth-promoting properties of this antibiotic.

Further studies of the effects of aureomycin on hepatic enzyme systems seemed warranted. Endogenous respiration, choline oxidase activity, choline dehydrogenase activity (using 2, 3, 5 triphenyl tetrazolium chloride) and citrate dehydrogenase were determined in the normal rat liver with and without the addition of aureomycin in vitro. The same enzyme systems were studied in rats given 20 mg. aureomycin parenterally for 5 days and in those whose diet had a 0.5% aureomycin content.

Aureomycin added to rat liver homogenates inhibited the choline oxidase system and endogenous respiration approximately 36%. This inhibition included a direct inhibition by aureomycin of choline dehydrogenase. Aureomycin parenterally administered inhibited endogenous respiration (25%) but not choline oxidase activity, while oral aureomycin did not seem to depress endogenous respiration or choline oxidase activity. The inhibition by aureomycin in vitro of the choline oxidase activity of homogenates from aureomycin-fed rats seems to exclude an in vivo adaptation by the choline oxidase system to aureomycin.

In contrast to the in vitro inhibition of the choline oxidase system by aureomycin, this antibiotic appeared to enhance the activity of citrate dehydrogenase of liver homogenates by about 50% of both control animals and those from animals on an aureomycin diet. The dehydrogenase activity of rat liver homogenates was significantly greater when both choline and citrate were added as substrate, than the sum of the activity of either dehydrogenase system alone.

The Antibiotic Activity in the Cerebrospinal, Pleural and Ascitic Fluid after Administration of Diethylaminoethyl Hydriodide of Penicillin. *Morton A. Goldman*, George Gee Jackson, Mark H. Lepper and Harry F. Dowling*, University of Illinois, College of Medicine, Chicago.

Penicillin G in ordinary doses does not enter the cerebrospinal fluid in an appreciable concentration. Diffusion into pleural and ascitic fluids varies among individuals. The diethylaminoethyl hydriodide of penicillin has been found to yield higher concentrations of penicillin in brain tissue and cerebrospinal fluid than those obtained with other penicillin salts and esters. In the present study, comparison was made between the concentration of penicillin in the serum and the concentration in a specimen of cerebrospinal, pleural or ascitic fluid which was obtained concurrently. Eleven of 13

patients given a dose of 500,000 units and all the patients who received a million units demonstrated 0.03 or more units of penicillin per ml. of the body fluids assayed. Among the latter group the mean penicillin level in the cerebrospinal fluid was 0.28 units per ml. and that for the ascitic and pleural fluid 0.63 and 1.8 units per ml. respectively. Any special tissue affinity of this preparation must depend on its transport as an ester and penicillin esters are not ordinarily biologically active. Since the usual bioassay technics activate the ester, the high levels observed may not reflect *in vivo* activity. To avoid activation during incubation, assays were performed at a pH of 4.9, using *Streptococcus lactis* as a test organism. Relatively little antibiotic activity was demonstrable in the serum. Through paper chromatography it was shown that part of the penicillin present after Neo-Penil, is distinguishable from penicillin G and presumably activated during *in vitro* incubation.

The Control of "Group A" Beta Hemolytic Streptococcal Disease by the Mass Use of Orally Administered Penicillin. *Stanley H. Bernstein*, O. F. Harper, Jr.*, William H. Klingensmith* and Jerome A. Cantor.* (introduced by *Harry A. Feldman*), Department of Preventive Medicine, USAF Epidemiological Detachment, 1141st Medical Services Squadron, Sampson Air Force Base, New York.

Penicillin was administered orally on a dosage schedule of 250,000 units, twice daily for 10 days to approximately 5,500 trainees at Sampson AFB during the winter of 1952-53 in order to determine the effect of such treatment upon the incidence of Group A beta hemolytic streptococcal carriers and infections. A similar group, comparable in service and numbers, but quartered separately on the same base served as untreated controls. Carrier surveys were performed on approximately 15% of the men prior to treatment and at weekly intervals thereafter. The incidence of carriers was 13% among the test group prior to treatment, 2% by the third day of treatment, 2% one day after discontinuing penicillin, 4% one week later and 5% the following week. Surveys performed among the control group demonstrated 13%, 15%, 13%, 12% and 14% carriers for the parallel dates.

The incidence of bacteriologically proven cases of Group A beta hemolytic streptococcal infections was 16.6/1000/week at the start of penicillin treatment and this declined among the treated group to 1.9, 1.4, 3.2 and 2.2 at the intervals indicated above. Among the controls, the initial rate was 10.5/1000/week and in subsequent weeks this was 13.3, 10.7, 11.9.

At the beginning of the fourth week, following the initiation of the 10-day treatment schedule, approximately $\frac{1}{3}$ of the control group, which could be separated readily from the remainder, received

250,000 units of penicillin twice daily for 5 days. Two days after completion of this course, this group was found to have 2% carriers in contrast to a pretreatment level of 16%. During the same period, the case rate declined from 15.6/1000/week to 1.3. Similar determinations were essentially unchanged among the controls.

Additional data will be presented concerning the effect of these schedules upon the occurrence of acute rheumatic fever and acute glomerulonephritis. Penicillin sensitivity reactions were few. There was no evidence that the drug caused any exacerbation of fungus infections of the feet.

The Relative Inefficacy of Penicillin Alone in Protecting Against Subacute Bacterial Endocarditis.

Robert S. Pressman, Northern Division of the Albert Einstein Medical Center, Philadelphia. (supported by a grant from Wyeth, Inc.).

A recent analysis of 442 cases of subacute bacterial endocarditis by Cates and Christie indicated 48% of these cases occurred with "a dental focus of infection or a history of a tooth extraction" and some "other focus of infection" in another 14%. Penicillin alone has been considered, heretofore, as the ideal agent in protecting against the bacteremia following the extraction of teeth. Our studies indicate that since the bacteremia originates in the mouth, the use of antibiotics must be aimed at the suppression of the salivary population count. Relatively little penicillin is excreted into the saliva when given parenterally in therapeutic doses insufficient to depress the population count. The same is true of streptomycin. However, when used in combination parenterally, in therapeutic doses, there is a 65% reduction in the bacterial population count. Blood cultures taken immediately following the extraction of two or more teeth after the parenteral administration of penicillin alone indicate a reduction from 82% in control cultures to approximately 40% in the cultures in penicillin treated patients. Using parenteral penicillin and streptomycin in combination, plus the addition of an antibiotic troche containing penicillin, bacitracin and Sulfadiazine, reduces the percentage of positive cultures from 82% in the control group down to 17.1% in this group. In Cates and Christie's series, the overall four year mortality, following subacute bacterial endocarditis, was 48%. Since the best treatment is always prevention, we strongly urge the administration of parenteral penicillin and streptomycin plus an antibiotic troche in all cases of the rheumatic diathesis prior to any dental or operative procedure.

The Effect of an Alumina Gel Vehicle on the Blood Level of a Triple Sulfonamide Preparation after Oral Administration. *Donald Berkowitz**, Hahnemann Medical College and Hospital, Philadelphia. (introduced by *George E. Farrar, Jr.*).

It is now generally accepted that triple sulfonamide mixtures have certain advantages over single sulfonamide preparations. Recently, Seifter has shown that aluminum hydroxide gel increases the intensity and duration of action of various drugs. This prompted us to study the effects of alumina gel as a suspension medium for triple sulfonamides.

Four sulfonamide preparations were studied. The compounds used were (1) Sulfose (a triple sulfonamide preparation containing sulfadiazine, sulfamerazine, and sulfamethazine suspended in alumina gel) (2) an identical preparation but without alumina gel (3) sulfisoxazole and (4) sulfadimetine, the latter two being single sulfonamides.

Four grams were given initially, with subsequent 1-gram doses every 6 hours in the case of the triple sulfonamide mixtures and sulfadimetine,

whereas sulfisoxazole was given in 2-gram doses every 6 hours. Free and total blood sulfonamide concentrations were determined at various times after initiation of therapy.

The triple sulfonamide-alumina gel mixture gave consistently higher blood levels than any of the other preparations. It reached a therapeutic blood level (10 mg.%) within two hours after the initial dose and maintained this level for 12 hours. None of the other preparations ever reached a therapeutic level. Furthermore, 76% of the patients receiving the alumina gel mixture had a therapeutic level after 6 hours, as opposed to 44% of those who received the identical mixture without alumina gel.

It would therefore seem that alumina gel is an effective agent for prolonging blood sulfonamide levels.

KIDNEY AND URINARY TRACT

Comparative Effects of Ambulation and Head-up Tilting on Renal Function and the Excretion of Water and Electrolytes. *R. V. Ford*, J. H. Moyer and C. L. Spurr*, Departments of Medicine and Pharmacology of Baylor University College of Medicine and the Department of Medical Research of the Veterans Administration Hospital, Houston.

During the course of investigation of autonomic factors in patients with hypertension, control values for renal functions and the excretion of water and electrolytes were determined before and after ambulation (7 patients) and passive 60° head-up tilt (20 patients). The data indicate that the hypertensive patient reacts as the normal patient to head-up tilting regardless of the presence or absence of impaired renal function. There was a decrease in renal plasma flow (to 72% of control), glomerular filtration rate (inulin clearance) (71% control), tubular excretory maximum (82% control), urine volume (50% control), sodium excretion (40% control), and potassium excretion (75% control), while the mean blood pressure dropped to only 90% of control. During ambulation, there was a decrease in RPF (82% control), GFR (88% control), TmPAH (89% control), urine volume (79% control), sodium excretion (74% control), potassium excretion (106% control), while the mean blood pressure was 101% of control. The renal vascular resistance increased to 130% of control during tilting and to 116% of control during ambulation. A patient with severe "salt-losing nephritis" demonstrated findings proportionately similar to the normal and hypertensive patients after tilting. Thus: (1) The ambulatory state is qualitatively similar to head-up tilting in its ability to increase

renal vascular resistance and to depress renal functions but is quantitatively less severe; (2) the decrease in water and sodium excretion exceeds the decrease in renal functions and was greatest in the tilt, suggesting greater vasoconstriction in this "unphysiologic" state; (3) potassium excretion apparently is more easily adaptable to changes in stress than is the rate of sodium excretion; and (4) there is rapid compensation for the depression of water and sodium excretion following return to the recumbent position.

Observations on Diurnal Variations in Fluid and Electrolyte Excretion. *William W. Schottstaedt*, Laurence E. Hinkle, Jr., and Harold G. Wolff**, Departments of Medicine and Psychiatry, New York Hospital-Cornell Medical Center, New York.

Studies of renal excretion of water, sodium, and potassium collected as 4 specimens daily to cover each 24 hours and extending over periods of 10 to 46 days have been performed on five healthy subjects carrying on their routine daily activities. Careful records of intake, activity, and feeling states were kept. The data collected suggest that the classic pattern of diurnal variation is present when a large number of observations are combined but that individuals may depart considerably and frequently from this pattern. Neutral or tranquil periods showed comparable rates of excretion of water and sodium at whatever time of day or night they occurred. Situations arousing feelings of apprehension and excitement were associated with a diuresis of water and sodium; those arousing anger or resentment, with a diuresis of sodium; those arousing tension or depression, with retention of water and sodium. These variations were of com-

parable magnitude at whatever time of day the feeling state occurred. The most consistent diurnal change was a decrease in potassium excretion at night, but this was frequently not observed when the subject was restless or dreaming. Where the classic pattern of diurnal variation was noted, the predominant feeling states on retiring were tension and depression; these states are associated with decreased rates of excretion at any time they occur. It is suggested that emotions and feeling states are factors in determining diurnal variations in fluid and electrolyte excretion.

Renal Conservation of Potassium by Normal Adult Males on Low Potassium Diets. *R. D. Squires, E. J. Huth* and J. R. Elkinton**, Chemical Section, Department of Medicine, University of Pennsylvania, Philadelphia.

Balance studies were done on 3 subjects. Control periods were 7 days in length. Depletion lasted 4 to 7 days on diets of 25 mEq. of potassium per day. Subject 1 was kept on an intake of 140 mEq. of sodium per day in both periods and a potassium intake of 110 mEq./day in the control period. Subject 2 was on a high sodium intake up to 300 mEq./day in the control period and kept at 272 mEq./day during depletion. His control potassium intake was 114 mEq./day. Subject 3 was on a high potassium intake up to 315 mEq./day in the control period. His sodium intake was 170 mEq. in both periods. Caloric intake per day was constant. Nitrogen intake varied no more than $\pm 5\%$.

In depletion, potassium losses were 2.7 mEq./Kg. B.W. in 7 days in Subject 1, 1.4 mEq./Kg. B.W. in 4 days in Subject 2, and 3.7 mEq./Kg. B.W. in 7 days in Subject 3. In Subjects 1 and 3, UV_K equalled potassium intake by the fourth depletion day. In Subject 2 the UV_K remained relatively constant at 33-39 mEq./day during 4 days of depletion, suggesting that sodium loading sustained the renal loss of potassium.

Comparison of excretion of potassium in urine and in stool during depletion showed that the normal kidney will effectively conserve potassium during marked dietary deprivation except with concomitant sodium loading. In the final analysis, stool losses take the major responsibility for negative potassium balance.

Alterations of Renal Hemodynamics and Water and Electrolyte Excretion Following Pitressin in "Physiologic" Doses. *Robert C. Taymor, J. Minor* and C. K. Friedberg*, Department of Medicine, The Mount Sinai Hospital, New York.

A study was made of the effect of intravenous administration of Pitressin upon renal function and water and electrolyte excretion in 13 experiments in 12 normal, water-loaded subjects. The individual dosage varied from 0.3 to 1.0 milliunits of Pitressin per Kg. of body weight. Clearance studies

for inulin and p-aminohippuric acid were done at 15- or 30-minute intervals and the simultaneous excretion rates for water, sodium, potassium and chloride determined.

The effects of Pitressin occurred in 3 phases: first a brief renal vasoconstrictor, then a more prolonged antidiuretic phase, followed by a rebound phase with renal hyperfunction.

The control glomerular filtration rate ranged from 55 to 149 cc. per minute, the mean being 107; following Pitressin there was a fall in filtration rate in 12 experiments, ranging from 12 to 66% with a mean of 51%. Control effective renal plasma flow ranged from 315 to 661 cc. per minute; mean was 437. After Pitressin, renal plasma flow fell in 12 experiments. The range of fall was from 11 to 88% with a mean of 53%. During persistence of antidiuresis and recovery therefrom, there was an associated rebound in both filtration and plasma flow in 11 experiments. Filtration rate increased from 11 to 218% (mean: 54%) and plasma flow from 11 to 87% (mean: 39%).

Urine flow fell markedly in all experiments following Pitressin. Control rates ranged from 8.8 to 16.4 cc. per minute, the mean being 11.9 cc. per minute. During antidiuresis the rates ranged from 0.7 to 3.7 cc. per minute with a mean of 1.9. Antidiuresis persisted for a variable period after filtration rate had returned to normal or above. The control values for sodium, potassium and chloride excretion ranged from 68 to 223, 26 to 148 and 42 to 128 microequivalents per minute respectively. Mean values for control sodium, potassium and chloride excretion were 141, 68 and 99 μ Eq. per minute respectively. Following Pitressin the excretion rates were 12 to 189 μ Eq. per minute for sodium (mean: 72), 5 to 149 μ Eq. per minute for potassium (mean: 30) and 5 to 155 μ Eq. per minute for chloride (mean: 67).

Influence of Plasma Salicylate Concentration on Urate Clearance in Man. *T. F. Yu*, Jonas H. Sirota and Alexander B. Gutman**, Department of Medicine, The Mount Sinai Hospital, New York.

Large doses of salicylate produce uricosuria, small doses cause urate retention and also inhibit Benemid uricosuria. To explain these observations, the renal clearance ratio, C urate/C inulin, was determined before and during salicylate infusion and C urate/C creatinine was determined for 18-20 hours after salicylate infusion.

In 4 gouty subjects with plasma salicylate concentrations brought to <10 mg.%, C urate/C_{in} was depressed 32% from a mean control of 0.067. At plasma salicylate concentrations of 10-17 mg.%, the C urate/C_{in} depressions disappeared. At plasma salicylate concentrations >20 mg.%, a mean peak C urate/C_{in} ratio of 0.225 was obtained; at the end of 18-20 hours, when salicylate concentrations

had fallen to 4-8 mg. %, depressions of C urate/C_{cr} below control values were again observed.

In 4 other gouty subjects, intravenous Benemid (20 mg./Kg.) given prior to salicylate increased the mean C urate/C_{cr} from 0.065 to 0.385. When plasma salicylate concentrations were then brought to 8-10 mg. %, the mean C urate/C_{cr} ratio dropped to 0.165. When the salicylate concentration was increased to 21 mg. %, this inhibition of Benemid uricosuria disappeared. Benemid administered during salicylate uricosuria produced no change in C urate/C_{cr}. Throughout these studies, significant alterations of glomerular activity were not observed.

It is concluded that the renal tubular reabsorption of filtered urate is enhanced at plasma salicylate concentrations <10 mg. %, resulting in urate retention and inhibition of Benemid uricosuria; tubular reabsorption of urate is depressed at salicylate concentrations >20 mg. %, resulting in increased urate excretion.

Effect of Hemodialysis on Cardiovascular Dynamics in Patients with Acute Uremia. *Paul E. Teschan*, Department of Hepatic and Metabolic Diseases, Army Medical Service Graduate School, Washington, D. C.

To determine whether reversal of the blood chemical abnormalities associated with acute uremia would result in improved cardiac function, 11 pairs of cardiac output and central blood volume determinations were performed in 8 patients by the T-1824 dye-injection method during 11 hemodialyses with the artificial kidney; stroke volume and peripheral resistance were calculated. Limits of significance were established by duplicate measurements obtained within 10 minutes of each other.

When measurements obtained within 30 minutes after the start were compared with those made within 30 minutes prior to the conclusion of each dialysis (interval about 5 hours), cardiac output rose significantly in 3 patients, fell in 2 and remained unchanged in 6. Peripheral resistance was significantly increased in 5 instances, decreased in 3 and unchanged in 3. Minimum central blood volume declined in a majority of instances, a change which was not paralleled by the maximum or average values. Pulse rate, pulse pressure and mean blood pressure increased in a majority of instances while stroke volume fell.

Within the limits of significance of these measurements it is demonstrated that cardiac function in patients with acute uremia is neither regularly improved nor impaired in the course of hemodialysis.

Changes in Acid-Base Balance of Uremic Patients during Hemodialysis. *John M. Weller, Roy C. Swan* and John P. Merrill*, Peter Bent Brigham Hospital and Harvard Medical School, Boston.

The changes in the acid-base balance during hemodialysis have been studied in 10 patients. Nine

patients had chronic renal insufficiency, and 1 had acute renal failure. Prior to dialysis, 9 of the patients had a serum pH below normal. All 10 patients had a primary metabolic acidosis with a diminished concentration of whole blood buffer base due to decreased concentrations of both the protein (hemoglobin) and bicarbonate anions. Nine patients had a diminished serum total base concentration and 3 had fixed acid excess. In 5 patients a secondary respiratory alkalosis was present.

Hemodialysis alleviated the acidosis; increased the concentration of buffer base, primarily by increasing the bicarbonate fraction; increased the concentration of serum total base; removed phosphate and nonchloride-fixed acids, but at the same time corrected hyponatremia. This is in contrast to conservative therapy, which does not reduce significantly the level of fixed acids and usually results in further hyponatremia. Secondary respiratory alkalosis when present persisted throughout dialysis, and in 3 of these patients a primary respiratory alkalosis was produced by correction of the metabolic acidosis. This slow readjustment of the respiratory center is due to the independence of acid-base balance of intra- and extracellular fluids. It is possible that this delay in the readjustment of the intracellular pH and cellular metabolism may explain the 24- to 48-hour lag following dialysis before clinical improvement is shown by the chronically ill, severely uremic patient.

On Diuresis of Nephrotic Edema. *John A. James and Jack Metcalf*, Department of Pediatrics, Harvard Medical School and The Children's Medical Center, Boston.

Very little data is available concerning electrolyte and water metabolism in ACTH-induced diuresis in the nephrotic syndrome. A 25-day electrolyte and nitrogen balance was therefore carried out on a 4-year old nephrotic child before and during a course of ACTH therapy with subsequent diuresis. Interim measurements of endogenous creatinine clearance, plasma volume, and antipyrin and thiosulfate space were also made.

The results confirm large loss of extracellular fluid as an important feature of diuresis. However, there was also a considerable loss of sodium from the intracellular compartment. Although the external potassium balance did not change significantly, diuresis was associated with a shift of potassium into the intracellular compartment.

Antipyrin and thiosulfate failed to define adequately total body water and extracellular water while edema was present, although reasonable values were obtained after diuresis. Plasma volume and serum water remained essentially unchanged. Endogenous creatinine clearance increased and ammonium excretion decreased during diuresis.

These observations suggest that significant changes in electrolyte balance may attend, but do

not precede, the diuresis induced by ACTH therapy. The data are consistent with the hypothesis of intracellular potassium deficiency in the nephrotic syndrome.

The Alteration of Renal Function in the Thyrotoxic and Post-treatment Hypothyroid State. *Charles L. Spurr*, Department of Medicine, Baylor University College of Medicine, and Veterans Administration Hospital, Houston.

A group of 7 thyrotoxic patients, average BMR (+)29%, I^{131} uptake 47% of 1 μ c. 48 hrs., was studied by differential renal function tests, glomerular filtration rate (GFR) inulin and creatinine, renal plasma flow (RPF), tubular excretory maxima (TmPAH) and comparative ratios. Post-treatment studies were made 3 to 6 months after 3 to 10 μ c. of I^{131} when the average BMR was (-)19% and the I^{131} uptake 11%. The results indicate a relatively high value for GFR (inulin, 140 ml./min.; creatinine, 127 ml./min.) and a proportional increase in TmPAH (112 mg./min.), with an elevation of RPF to an average of 1090 ml./min. In the post-treatment period, there was a proportional decline in function. The GFR (inulin) decreased an average of 66.8% of control hyperthyroid state. The GFR (creatinine) was 72%, RPF 67.6%, TmPAH 78% of the control level. The filtration fraction was not altered and the GFR/Tm \times 100 ratio was 90% of the pre-treatment level. These data suggest that the thyrotoxic state is associated with an increase in circulatory dynamics, as measured by renal plasma flow, and concurrent increases in other functions as GFR and TmPAH which, because of their constant proportional change, may be largely dependent on the increased blood flow. These changes revert toward normal upon control of the thyrotoxicosis.

Mechanisms of Electrolyte Imbalance in Patients with Ureterocolostomy. *Belding H. Scribner**, *John E. Lucas** and *James Cailoute** (introduced by *Robert S. Evans*), Veterans Administration Hospital and Department of Medicine, University of Washington, Seattle.

Unpleasant low-protein, low-chloride diets are advocated as part of the treatment for hyperchloremia and acidosis in patients with ureterocolostomies. To investigate the causes of this hyperchloremia and acidosis, a variety of solutions, including human urine, were introduced into an isolated loop of human transverse colon. After one hour each solution was withdrawn and analyzed to determine the amount of chloride absorbed in excess of sodium, potassium and calcium. This excess chloride absorption measures the tendency of the solution to cause hyperchloremia and acidosis.

Normal saline, acid sodium phosphate, acid and neutral urine had a high excess chloride absorption due to the secretion of potassium and bicarbonate and the absorption of sodium and chloride. Rapid absorption of ammonium chloride gave solutions containing a very high excess chloride absorption.

Excess chloride absorption could be reversed by introducing an alkaline, bicarbonate-containing urine. This reversal was not changed by the addition of ammonium bicarbonate used to simulate the effect of urea splitting.

All solutions, despite their initial potassium concentrations as high as 78 mEq./L., picked up potassium while in the loop. This may explain the severe hypokalemia reported in some ureterocolostomy patients.

These studies suggest that hyperchloremia is due to selective reabsorption of chloride from urine in the colon caused by ion exchange of chloride for bicarbonate plus ammonium chloride reabsorption. The acidosis is due to nullification in the colon of the normal renal acid-producing mechanisms: ammonia production, titratable acidity production and bicarbonate conservation.

Since alkali therapy cures acidosis and causes bicarbonate to appear in the urine, and since bicarbonate in the urine reverses excess chloride reabsorption in the colon, alkali therapy alone should correct hyperchloremia and acidosis in ureterocolostomy patients. Preliminary trial using sodium citrate has been successful in 2 cases.

LIVER

Responsiveness to the Pancreatic Hyperglycemic Glycogenolytic Factor (HGF) as a Test of Liver-Function. *R. F. Kibler** and *J. D. Myers*, Duke University School of Medicine, Durham.

Previous studies utilizing the technic of hepatic venous catheterization have demonstrated that the hyperglycemic effect of HGF is produced by an increase in hepatic glucose production, presumably by glycogenolysis. In contrast to a similar action of epinephrine, this effect of HGF is not associated with other obvious metabolic or circulatory changes.

It seemed reasonable, therefore, that the hyperglycemic response to HGF might prove a clinically useful hepatic function test and be superior to the previously used epinephrine test. Consequently, the responses to HGF in a group of patients with hepatic disorders have been compared with results in a group of control subjects.

In 9 control subjects, following 3 mg. of HGF intravenously, the mean rises in arterial blood glucose concentrations were: 5 min., 19 mg.%; 10 min., 21 mg.%; 15 min., 16 mg.%; and 20 min., 13 mg.%.

Sixteen patients with clinically moderate to severe hepatitis or cirrhosis, similarly treated, had mean elevations of not more than 5 mg.% at any time. The differences in mean elevations between the two groups at each specified time interval are statistically highly significant ($p < 0.01$). In striking contrast, 5 patients with marked extrahepatic ductal obstruction showed normal responses.

In many patients the response to HGF was a valuable guide to the proper diagnosis. Moreover, in several cases in which an incorrect clinical diagnosis had been made with the aid of conventional liver function tests, the HGF response was indicative of the proper and finally proven diagnosis.

It is concluded that the hyperglycemic response to HGF may be a clinically useful hepatic function test.

Study of Several Factors which may Influence Serum Cholinesterase. *David W. Molander*, Pack Medical Foundation, New York. (Supported by funds received from the Lilla Babitt Hyde Foundation.)

In an effort to determine the effect of anemia on the serum cholinesterase level of white rats with intact parenchymal liver function, a group of animals was repeatedly bled and an equal volume of serum which was withdrawn was reinjected at each bleeding; thus the serum protein level was not impaired. The standard liver function tests were repeated at intervals. It was found that a marked anemia can be present, yet the serum cholinesterase and other liver function tests need not necessarily be altered, providing that the serum protein levels are relatively normal.

In another group of rats, protein levels were depleted by repeatedly bleeding animals and the red cell mass was maintained constantly by reinjection of the red cells at each bleeding. Depression of serum cholinesterase levels appeared to be uniform and roughly seemed to parallel serum albumin levels.

In a third group of animals, parenchymal liver damage was produced by carbon tetrachloride administration. The serum cholinesterase and other liver function tests were periodically performed as well as liver biopsies.

Serum cholinesterase levels proved to be a useful, reliable index of parenchymal liver function. The ease of determination of this material by a colorimetric procedure, seemed to be a definite advantage of this test over other more laborious liver function tests.

Comparison of Flocculation and Bromsulphalein Tests in Cirrhosis of the Liver. *Irving B. Brick*, Department of Medicine, Georgetown University Medical Center, Washington, D. C.

Comparison of cephalin flocculation, thymol turbidity and bromsulphalein tests is made in 112

cases of hepatic cirrhosis, the diagnosis of which in all cases is confirmed microscopically on specimens of the liver obtained by needle biopsy. These tests were selected for this study since their use is widespread and simple of application in office or hospital laboratory. The cases are divided into jaundiced and nonjaundiced groups in comparing the tests, and some interesting differences are noted. Correlation of abnormal bromsulphalein retention and diagnosis of cirrhosis is excellent, whereas the correlation of the flocculation tests with presence of cirrhosis is not nearly as accurate. In other words, a not inconsiderable percentage of the cases of cirrhosis is shown to have normal values of the flocculation tests studied. In the jaundiced cases of cirrhosis, correlation of the flocculation tests is somewhat better.

Whereas 83.1% of the nonjaundiced cirrhotic cases had an abnormal bromsulphalein retention, only 27.2% and 36.3%, respectively, had abnormal cephalin flocculation and thymol turbidity tests. In the jaundiced cases, the cephalin flocculation test was positive in 57.1%, and the thymol turbidity in 71.4%. Dependence on flocculation tests for diagnosis of cirrhosis is shown to be unreliable. It is apparent that histologic and functional correlation with the tests used is far from exact.

The Liver in Chronic Alcoholism: A Clinical and Pathologic Study. *Gerald B. Phillips, Dante Campagna-Pinto,* Frederic Parker, Jr.,* and Charles S. Davidson.* Thorndike Memorial Laboratory, Boston.

The clinical manifestations and hepatic histology of 56 chronic alcoholics with liver disease were examined. Characteristic histologic abnormalities consisting of severe degrees of (1) parenchymal disorganization, (2) intracellular hyalin (Mallory), and (3) liver cell necrosis were observed in 17 cases who died. An almost constant feature of this pathologic picture was fibrosis. In addition, there was usually hepatic fat, but the characteristic lesions appeared to be independent of the amount of fat present. Of these 17 patients, 10 were female, all but one were jaundiced, often with acholic stools, most had progressive polymorphonuclear leukocytosis, and all died in spontaneous hepatic coma.

Of the remaining 39 patients, most of whom lived, 12 showed the same lesions in moderate to marked degree in liver punch biopsy specimens. Lesser degrees of the lesions were usually not fatal and were associated with lesser degrees of hepatic functional impairment.

Hepatic fat and fibrosis, alone or in combination, were seen frequently without the characteristic histologic lesions and were usually associated with less severe clinical manifestations and a better prognosis.

It is concluded that in chronic alcoholics, a typical hepatic lesion characterized by parenchymal

disorganization, intracellular hyalin, and necrosis occurs, which is distinct from the fatty lesion and is usually responsible for the acute severe liver impairment which seems to have a predilection for females and often leads to fatal coma.

Changes in Body Potassium in Hepatic Decompensation. *Belton Burrows, Jane Denton,* Bruce Ferguson* and Joseph Ross*, The Radioisotope Unit and Medical Service, Boston Veterans Administration Hospital and the Robert Dawson Evans Memorial, Massachusetts Memorial Hospital, Boston.

The tissue-wasting and low-sodium edema of decompensated hepatic cirrhosis may be associated with potassium depletion. Repeated measurements by the isotope dilution technic of "exchangeable potassium" were performed over periods of 1 to 14 months on patients admitted with hepatic decompensation. Eight of the 12 patients studied initially had a low serum sodium concentration, ranging from 120 to 135 milliequivalents per liter, with fluid retention in addition to other clinical and laboratory evidence of severe liver disease. Serum potassium concentrations were within the normal range.

Initial "exchangeable potassium" values, related to total body weight at the time of the study, ranged from 23 to 41 mEq./L., or from 50 to 90% of the normal average for males. The initial "exchangeable potassium" bore no relationship to prognosis, in that patients with values in the lower range improved and patients with initial higher values pursued a downhill course. Clinical improvement, with a diuresis of accumulated fluid and a return of the serum sodium concentration to normal values, was in general associated with an increase in "exchangeable potassium," although improvement might become evident before the increase in "exchangeable potassium."

Even in instances where the "exchangeable potassium" was reduced initially by 25%, it was restored to normal values with significant improvement in the hepatic function and nutritional state of the patient. The return of serum sodium to normal before any significant increase in "exchangeable potassium" occurred suggests that the phenomena are not interdependent.

Antidiuresis and Hyponatremia in Cirrhosis of the Liver. *Robert Schwartz, George J. Gabuzda, Jr., and Charles S. Davidson*, Thorndike Memorial Laboratory, Boston.

Sodium retention and delayed water excretion frequently accompany cirrhosis. The extent to which these factors contribute to the hyponatremia of some patients with ascites and edema was investigated in nine alcoholics with cirrhosis, given constant diets. Wide variations in fluid (1-4 liters daily) and sodium intake (10-113 mEq. daily) were made independently, each regimen being maintained for

several days. Body weight and serum and urinary electrolytes were measured. At the time of chronic water loading, five patients excreted virtually sodium-free urine, one was beginning sodium excretion, two were in the midst of sodium diuresis, while one had just completed a diuretic phase.

Variable responses to the chronic water loading were noted. These bore no apparent relationship to the ability to excrete sodium. Of the patients with marked sodium retention, two gained weight and developed hyponatremia when given water loads although weights were previously constant on minimal sodium intakes. Another, who excreted small amounts of sodium, responded similarly. One patient who maintained weight while ingesting 113 mEq. sodium daily, gained weight with water loading, but did not develop hyponatremia. Five of the 9 patients studied, excreted the water load and had no change in body weight or serum sodium, although three of these patients who were given sodium chloride gained weight.

Conclusions: Sodium and water retention in cirrhosis can be independent phenomena. When the intake of sodium is limited and water excessive, increases in body weight and hyponatremia may occur. This hyponatremia can best be interpreted as dilution related to increased antidiuretic activity. Cellular shift of sodium need not be postulated.

The Clinical Significance of the Blood Volume in the Anemia of Portal Cirrhosis. *Robert B. Chodos, Jane Denton*, Bruce Ferguson and Joseph F. Ross*, Radioisotope Unit and Medical Service, Veterans Administration Hospital, Boston.

The anemia of portal cirrhosis is obscure as to its nature and pathogenesis. It has been postulated that this is primarily an anemia of hydrema while others maintain that this anemia represents a true decrease in circulating red cell mass. This study was designed to more clearly delineate the changes that occur in blood volume and circulating red cell mass and to correlate these changes with the clinical course of the patients. Sixty-five blood volume determinations by the radioactive phosphorus tagged red cell method were serially performed at frequent intervals on eleven patients with moderate to severe portal cirrhosis during a period of observation ranging from 1 to 14 months. These observations revealed that the total circulating hemoglobin was significantly decreased in a majority of the patients and that clinical and laboratory improvement was accompanied by an increase to or toward normal levels of total circulating hemoglobin. The hemoglobin concentration (in Gm.%), however, did not always reflect the level of total circulating hemoglobin or its variation during the course of the patient's illness, since concomitant alteration of the plasma volume did indeed influence the relative concentration of hemoglobin. Elevated plasma volumes were observed in asso-

ciation with a decrease in relative concentration of hemoglobin. We therefore conclude that the anemia of cirrhosis usually represents an absolute reduction in the total red cell mass, with the additional observation that elevation of the plasma volume may contribute to a relative reduction in the hemoglobin concentration.

Relationship of Esophageal Varices and Spider Angiomata in Cirrhosis. *Irving B. Brick and Eddy D. Palmer,** Department of Medicine, Georgetown University Medical Center, Washington, D. C.

One hundred and fifty patients with cirrhosis, demonstrated by microscopic examination of specimens of the liver, were routinely esophagoscoped to determine the presence of varices. In 95 of these patients varices were present. In correlating the physical findings in these cases, spider angiomata were found in 75 cases or 50% of the whole group. However, the striking feature was that angiomata were present in 59 cases of the 95 that had varices demonstrated—an incidence of 62%. This contrasts with the 16 cases with spiders in the 55 patients without varices, or an incidence of 20%. Since spider angiomata were found three times more frequently in cirrhotics with esophageal varices, it would appear that in addition to being a diagnostic finding of significance, the presence of angiomata should arouse suspicion of the presence of esophageal varices. Other physical findings such as hepatomegaly, ascites, and splenomegaly did not show any striking differences as between the presence or absence of esophageal varices.

The cause of spider angiomata in liver disease is not completely known. Bean has postulated difficulty in metabolism of estrogens as being a possible explanation. The distribution of spider angiomata, practically always above the level of the diaphragm, has eluded explanation. The findings in the present study are suggestive of portal hypertension being a causative or correlative factor in view of the high incidence of spider angiomata with esophageal varices which nearly always indicates

marked portal hypertension. The presence of spider angiomata in cirrhotics without esophageal varices may indicate lesser degrees of portal hypertension than are found with varices.

The Effect of Portacaval Shunt on Liver Function.

Victor M. Sborov, Edward S. Jahnke, Jr. and William S. Sharon,** Department of Hepatic and Metabolic Diseases, Army Medical Service Graduate School and Department of Surgery, Walter Reed Army Hospital, Washington, D. C.

As part of a general program to evaluate the portacaval shunt operation in the prevention of bleeding from esophageal varices, liver function has been studied in a baseline period prior to surgery and for a varying period following the operation. Twenty-one patients with an end-to-side portacaval anastomosis and 5 patients with a spleno-renal anastomosis were studied for a mean of 4½ months after surgery. Significant worsening of hepatic tests was noted in all of the patients having the end-to-side portacaval operation and in 3 of the 5 having the spleno-renal shunt.

Characteristically, the serum bilirubin (1 min. and total) rose the day following surgery and remained above the preoperative levels for a mean of 31 days. In all but 4 cases there was a drop in thymol and zinc turbidities immediately following the operation. These did not return to the preoperative levels for 2 to 4 weeks. The explanation for this latter finding is not clear. In 12 patients a drop was noted in the serum albumin of 0.5 Gm. or more with a rise in the globulin fraction. The serum albumin levels tended to be lowest in the first month after surgery; thereafter they returned toward their preoperative levels. Peripheral edema and ascites were associated with the low albumin.

Three patients in this series died in liver failure. One died 5 and another 46 days postoperatively. The third died 10 months after operation. All others have survived. No correlation could be seen between the hepatic functional status prior to surgery and the morbidity or the mortality of the shunt operation in this small series.

METHODS

Simple Clinical Electrophoretic Analysis of Proteins in Body Fluids. *G. R. Cooper, L. A. Smith* and R. H. Owings,** Communicable Disease Center, Public Health Service, Federal Security Agency; Department of Medicine of Emory University School of Medicine; and Grady Memorial Hospital, Atlanta.

A simple paper electrophoresis instrument was built for routine use in clinical investigations. It is a modification of the horizontal type introduced by Kunkel and Tiselius and consists of electrode plexi-

glass compartments and a horizontal bridge constructed with a bottom glass plate and an elevated top plastic plate with an opening over starting positions. Tests upon 20 different filter papers reveal that Whatman 3MM paper gives best analyses and that 4 other papers are acceptable. An inexpensive power pack is satisfactory for 6 to 12 simultaneous determinations and an automatic scanning and recording device permits quick analyses.

Studies upon technic indicated that a stable starting spot is formed by adding the protein to the

paper through the opening in the top plate after fluid equilibrium is attained. Drying the paper before staining always disturbs the pattern to some extent. Analysis of a standard serum with each run is a good control. Serum is used undiluted, but urines and spinal fluids are concentrated 50 times by dialysis in a cellophane bag against 20% dextran solution while ascitic, pleural and pericardial fluids are concentrated twice.

Paper electrophoresis appears particularly useful when the serum total protein values are outside the normal range, when the presence of abnormal proteins such as cryoglobulins is suspected, for the differential diagnosis of multiple myeloma, cirrhosis, nephrosis or amyloidosis, and for the analysis of body fluids other than blood.

The Use of an Ion Exchange Column for the Simultaneous Measurement of Exchangeable Sodium and Potassium Spaces in Man. *Walter L. Arons,* Robert J. Vanderlinde* and Arthur K. Solomon** (introduced by *Frank H. Gardner*), Boston.

An ion exchange resin column (Dowex 50, 12% cross-linked, -325 mesh, 9 cm. in length) has been utilized to separate the sodium and potassium of the serum in order to measure simultaneously exchangeable sodium and potassium spaces in man. Separation of these cations by this method has proved to be complete and is felt to be superior to standard chemical separations because of its technical simplicity. Twenty-four hours following the intravenous injection of tracer amounts of radioactive sodium and potassium, a serum sample is drawn. After precipitation of the serum proteins with 10% trichloroacetic acid, sodium and potassium are separated on the resin column by means of differential chromatographic elution with 0.3 N HCl. The specific activities of the two fractions are then determined, and, after correcting for urinary losses, the exchangeable sodium and potassium spaces are calculated by means of the standard isotope dilution formula.

This method has been used in determining exchangeable sodium and potassium spaces in normal young adult subjects of both sexes. Successive determinations in the same patients have shown the method to be highly reproducible. In addition, studies of several metabolic states have been made. The effect of various adrenal cortical hormones on

the exchangeable sodium and potassium spaces has been investigated in patients on metabolic balance, and a comparison made with external balance data. Sodium and potassium space determinations have also been carried out in a group of patients with hypothyroidism before and after thyroid therapy.

Distribution and Fate of a Finitely Soluble Colloid: Intravenously Administered Radioactive Colloidal Palladium Iodine (I^{131}). *Frank J. Kelly, Royal H. Benson* and Isaac D. Welt,** Radioisotope Unit, Veterans Administration Hospital and Department of Medicine, Baylor University College of Medicine, Houston.

Radioactive diiodofluorescein, tetra-iodo-phenolphthalein, colloidal gold, silver iodide and palladium iodide have been used to obtain outlines of the liver by methods previously reported for the outlining of the thyroid. Only colloidal gold and colloidal palladium iodide gave satisfactory outlines in the amounts used (1-2 mg. of PdI_2^{131} containing 0.5-1.0 mc. I^{131}). Since the latter is more rapidly eliminated from the body, it was the compound of choice. Outlines of liver, lung and spleen, are obtainable 30 min. after injection.

Detailed analysis of blood regression, tissue distribution and excretion have been done in 9 dogs and 1 terminal patient. Initial behavior and localization in the R-E system is similar to that reported for other colloids. Following a minimum at 30 minutes, the blood concentration rises as dissociation occurs. This finite solubility is reflected by thyroid uptake and urinary excretions of I^{131} . The EBT $\frac{1}{2}$ in the liver is 1.2 days and it is considerably longer in the whole animal unless the thyroid is blocked.

Irregular particle distribution in the normal liver precludes the clinical use of such outlines for the localization of small tumors. However, the behavior and density of this compound suggests its trial as a contrast medium, if tolerated in sufficiently large quantities. Furthermore, this compound may be used more safely than colloidal gold for tumor therapy, since, if inadvertently injected intravenously, it is rapidly eliminated from the body. This type of compound offers a new method of studying the physiology of the R-E system.

NEOPLASTIC DISEASE

The Role of Pituitary Hormones in Liver Cancer Development. *A. C. Griffin,* A. P. Rinfret,* C. R. Robertson* and M. O'Neal** (introduced by *P. H. Forsham*), Division of Biochemistry, School of Medicine, Stanford University, California.

It has recently been established in this laboratory that hypophysectomy effectively inhibits the formation of liver tumors in rats fed diets containing the carcinogenic azo dyes. Normal rats maintained on such diets for 10-12 weeks have extensive liver damage and severe cirrhosis. After 20 weeks, how-

ever, the hypophysectomized rats still had normal livers and no tumors were evident. A study has been made to determine at what stage the carcinogenic process may still be reversed by hypophysectomy. Normal animals maintained on the diet containing the azo dye were hypophysectomized at varying time intervals. Hypophysectomy up to 7 weeks completely inhibited tumor development. After this period of azo dye feeding, removal of the pituitary was far less effective in blocking the carcinogenic process.

Groups of hypophysectomized rats fed diets containing the carcinogenic azo dye were treated with various pituitary and adrenal fractions. ACTH and also a crude pituitary gonadotrophic fraction partially restored the carcinogenic process. Hypophysectomized rats injected with cortisone, desoxycorticosterone acetate, testosterone, and certain pituitary fractions were still immune from the action of the azo compounds. Studies are now in progress to determine if growth hormone, thyrotropin or purified gonadotrophic fractions are directly involved in the reactions that lead to liver cancer development.

Response of the Various Cell Types of Bronchogenic Carcinoma to Nitrogen Mustard Therapy. *Bennett Levine* and Austin S. Weisberger*, Department of Medicine, Western Reserve University School of Medicine, Cleveland.

Although nitrogen mustard is beneficial in some cases of bronchogenic carcinoma, many patients fail to receive any significant benefit. A comparison was made between the cell type and the response to nitrogen mustard therapy in 31 cases of bronchogenic carcinoma. Eleven of the 31 patients had small cell carcinoma of the lung, the remaining had either squamous cell carcinoma, adenocarcinoma or anaplastic carcinoma of the lung.

Ten of the 11 patients with small cell bronchogenic carcinoma had significant improvement following nitrogen mustard therapy. In these patients there was rapid striking improvement with disappearance of masses, increase in appetite and gain in weight and strength. Objective evidence of regression in the size of the primary tumor was apparent by serial roentgenographic examination in 4 patients. Evidence of regression of liver metastases was apparent in one instance by decrease in hepatomegaly and disappearance of jaundice. Decrease in venous pressure from mediastinal compression was observed in 1 case and improvement in neurologic signs from cerebral metastases was observed in 3 cases. None of the patients with other types of bronchogenic carcinoma demonstrated any significant improvement following nitrogen mustard therapy. In 2 patients, there was a slight decrease in the amount of pain, but no other signs of improvement were observed.

The origin of small cell carcinoma of the lung

has been disputed. It has at times been classified as a lymphosarcoma. The response of this tumor to nitrogen mustard therapy may indicate that it is a lymphosarcoma rather than carcinoma.

Effect of Triethylene Melamine on Bone Marrow Involvement in Chronic Lymphocytic Leukemia. *W. B. Barton,* Evelyn V. Coonrad* and R. W. Rundles*, Duke University School of Medicine, Durham.

The important causes of disability and ultimate fatality in chronic lymphocytic leukemia— anemia, infection and hemorrhage—result from replacement of the bone marrow by infiltrating or proliferating lymphocytes. The possibility of preventing marrow involvement, and of reversing it when present, by sustained TEM therapy was studied in 49 patients.

Nine patients had no marrow infiltration at the start of therapy. Three did not respond to TEM, or to other agents, and progressed to a fatal termination. In 6, objective evidence of disease subsided, and their bone marrows remained normal during observation periods of 5-16 months.

Twenty patients had marrow infiltration without cytopenia at the beginning of therapy. One was not benefited and 3 died of apparently unrelated causes. In 16, evidence of disease diminished or disappeared, and they remain asymptomatic after observation periods of 3½-30 months. Marrow infiltration remained unchanged in 4, lessened in 6, and disappeared in 4. Follow-up studies are unavailable in 6.

Six patients had heavy marrow infiltration with hemoglobin levels initially of 7.5-11.4 gm.%. One was not benefited by any therapeutic agent. In 5, the hemoglobin level became normal. Marrow infiltration lessened in 3, and disappeared in 2.

Fourteen patients had leukemic marrow replacement, with hemoglobin below 7 gm.%. Marrow infiltration disappeared in 2 and anemia subsided for 7 and 20 months, respectively. In 12 there was no improvement and the majority lived but a few weeks or months.

In the majority of patients with chronic lymphocytic leukemia, lymphocytic proliferation can be effectively suppressed by TEM. The efficiency of this chemical, most critically judged by its effect on bone marrow cytology and function, appears to be superior to other agents studied.

Metabolic Effects of a Metabolite Antagonist (dl-ethionine) in Man. *Laurens P. White* and Michael B. Shimkin** (introduced by Robert R. Commons), The Laboratory of Experimental Oncology, National Cancer Institute, National Institutes of Health, Public Health Service, Federal Security Agency and Department of Medicine and Cancer Research Institute, University of California School of Medicine, San Francisco.

In various mammalian species, dl-ethionine, has been shown to produce marked biochemical and pathologic disturbances. Among the pathologic changes noted in animals treated with this substance has been virtually total destruction of pancreatic acinar tissue. Applied to man, such a material could prove useful in the treatment of carcinoma arising from pancreatic acinar tissue, were such a carcinoma to retain most of the identity of normal acinar tissue. Five patients with far advanced carcinoma, including 3 with carcinoma of the pancreas, were therefore treated with dl-ethionine.

All patients were placed on a diet devoid of animal protein, the main source of nitrogen being vegetable protein of low methionine content. After several weeks of this regimen, during which baseline studies were performed, dl-ethionine was administered orally in doses of 0.6 to 1.0 Gm. per Kg. over periods of 1 to 6 days. During and following this time a broad spectrum of biochemical studies was performed and serial liver biopsies were obtained. All patients showed deterioration in liver function, with accompanying changes in the appearance of the liver. Patients on low methionine diets also developed albuminuria, leucopenia, dermatitis and toxic psychosis of variable severity. One patient developed acute yellow atrophy of the liver after receiving 40 Gm. of the drug.

The mode of action of this highly toxic material will be discussed. Its effects, both physiologic and pathologic, will be presented.

Thyroidectomizing Dose of Radioactive Iodine in Humans with Malignant Melanoma. *Levona W. Olmsted and William H. Beierwaltes*, University of Michigan, Ann Arbor.

Varied effects on tumor growth have been reported from total thyroidectomy in experimental animals. Total thyroidectomy has not been evaluated in the treatment of human melanomas. In the experimental animal, tumors have been reported to pick up more I^{131} -labelled diiodotyrosine and retain I^{131} -labelled thyroxine longer than nontumorous tissue.

Radioactive iodine was used to totally thyroidectomize five humans with histologically proven malignant melanotic melanoma to evaluate (1) the effect of total thyroidectomy on melanoma growth, and (2) the uptake of I^{131} and biosynthetically labelled radiothyroxine in melanoma as compared to gastrocnemius muscle. After the administration of 60-100 mc. of radioactive iodine, single or multiple metastases were excised and calf muscle biopsy obtained simultaneously on the first, third, and fifth day respectively in 3 patients, and on the fifth and eighth day on a fourth patient. Absolute beta assays of these specimens revealed ratios of melanoma I^{131} content to muscle I^{131} content of 2.7:1, 5:1, 25:1, 2.7:1, 21.5:1, and 12:1. The thyroxine I^{131} fraction was less than half the total I^{131} content in 5 of 6 tumor specimens. No constant radiothyroxine percentage was noted in muscle. During follow-up periods of 3 months or more, no change in rate of tumor growth was observed regardless of tumor I^{131} :muscle I^{131} ratio or completeness of thyroidectomy.

RESPIRATORY SYSTEM

Pulmonary Mechanics in Emphysema. *Inga Lindgren,* Jere Mead,* Edward A. Gaensler and James L. Whittenberger*, Dept. of Physiology, Harvard School of Public Health and Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital and Department of Medicine, Harvard Medical School, Boston.

The elastic and resistive properties of the lung were studied in 16 patients with advanced pulmonary emphysema. The transpulmonary pressure was measured with an intraesophageal balloon, the rate of air flow with a pneumotachograph and the respiratory volume by electric integration of the rate of flow. The elasticity of the lung was expressed in terms of compliance as volume change per unit of pressure change. The resistance of the lung, including airway and tissue resistance, was recorded in terms of pressure change per unit of rate of flow. The clinical diagnosis of emphysema was confirmed by conventional pulmonary function

studies including determination of maximum breathing capacity, timed vital capacity, resting and exercise spirometry, residual volume, and intrapulmonary mixing index. The mean compliance for the entire group was nearly the same as for a group of 23 normal subjects. However, the range in the group with emphysema was wider. Values below the lower range of normal were found only in patients with cor pulmonale and failure. During rapid respiration there was a striking decrease in compliance, a change not observed in normal subjects. The pulmonary resistance during quiet breathing was about 5 times larger than in the normal group and during expiration it was considerably greater than during inspiration. No such difference was found in normal individuals. During maximal expiratory efforts the resistance was further increased, 20 to 150 times, in striking contrast to the normal group. The theoretic implications of these findings will be discussed.

A Technic for the Measurement of Pulmonary Compliance and Resistance: Its Application to Normal Patients and Patients with Mitral Stenosis.

Jere Mead, N. Robert Frank,* Inga Lindgren,* Edward A. Gaensler and James L. Whittenberger, Dept. of Physiology, Harvard School of Public Health and the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital and the Department of Medicine, Harvard Medical School, Boston.*

Simultaneous recordings of the tidal volume, rate of air flow and intraesophageal pressure variations were made in spontaneously breathing individuals. Analysis of these variables permitted calculations of pulmonary compliance and resistance. Pulmonary compliance is an expression of the elastic properties of the lung; resistance is an expression of the air flow and tissue resistive properties of the lungs. The mean compliance in 23 normal subjects was found to be 0.20 ± 0.07 liter per cm. of water. During inspiration, pulmonary resistance was 1.7 ± 0.6 cm. of water at 1 liter/sec. flow. Significant direct relationships were observed between compliance and vital capacity, height, and body surface area. Resistance was inversely and less significantly related to these measurements. In 11 patients with rheumatic heart disease, in whom mitral stenosis was the predominant valvular lesion, compliance was 0.11 ± 0.05 liter per cm. of water. The average value was 0.12 ± 0.05 among the 8 compensated patients and 0.08 with a range of 0.06-0.12 among those in decompensation. Two patients without disability had normal ventilatory function as measured by conventional tests; however, their compliance was reduced to 0.11. Resistance was 2.9 ± 1.4 cm. of water at 1 liter/sec. flow for the entire group. It was 2.3 ± 0.8 among the compensated patients and 4.7, with a range of 4.0-5.6, among the 3 patients in circulatory failure. The slight increase in resistance, observed among compensated patients, was not apparent from the maximal breathing capacity, fractions of the total vital capacity expelled per unit of time, or the air velocity index. The well-established increase in resistance among patients in circulatory failure was only suggested by the changes in these conventional tests.

The Use of Endotracheal Pressure Recording as an Indicator of Elevation of the P_{CO_2} During Thoracic Surgery. *William W. Stead, F. E. Martin and John Middlebrook,* Veterans Administration Hospital, Minneapolis.*

In a study of alveolar ventilation during thoracic surgery, the common occurrence of respiratory acidosis was confirmed. The respiratory rate, rhythm and pressures were recorded by means of a strain gage and Sanborn recorder through a polyethylene tube inserted through the lumen of the endotracheal tube. During pauses in the administration of the

intermittent positive pressure of respiratory assistance, two distinct patterns were noted: (1) a flat pressure curve, indicating apparent apnea and (2) rhythmic negative pressure fluctuations, indicating spontaneous respiratory efforts by the anesthetized patient. (A combination of pentothal and curare was used in this series.) Further study revealed that whenever the pattern of apnea occurred the P_{CO_2} was normal or below. When there were spontaneous pressure fluctuations during the pauses the P_{CO_2} of the arterial blood was invariably above the patient's customary level. The threshold for spontaneous respiratory efforts varied somewhat between individuals and also with the depth of anesthesia. The pattern could be abolished by depths of anesthesia which are rarely attained clinically. The highest threshold found in 84 determinations on 14 patients was a P_{CO_2} of 55 mm. Hg. Previous studies during thoracic surgery had demonstrated the almost consistent occurrence of P_{CO_2} levels appreciably higher than this.

After the above facts were noted, several cases were studied with the anesthesiologist following the endotracheal pressure recording during pauses in his respiratory assistance. By this means the P_{CO_2} could usually be maintained near normal with relative ease. When the anesthesiologist was unable to furnish sufficient ventilation early in the procedure, the surgery was delayed while he corrected the acidosis. If he was unable to restore the normal P_{CO_2} by such specific efforts the operation was discontinued rather than take the risk of progressive acidosis.

Conclusion. A practical indicator of an elevated P_{CO_2} during thoracic surgery has been described.

An Electro-Mechanical Substitute for the Human Respiratory Center. *George A. Saxton, Jr.,* and George H. Myers* (introduced by Lewis Dexter), Medical Clinic, Peter Bent Brigham Hospital and Department of Medicine, Harvard Medical School, Boston.*

In order to insure the proper degree of alveolar ventilation in patients with respiratory paralysis, an automatic regulator was designed to control the pressure excursions of a mechanical respirator in accordance with the alveolar P_{CO_2} sampled from the patient's expired air. This device performed the following functions in this sequence: (1) Alveolar air was sampled and analyzed continuously by infrared absorption during each expiration (2) This reading in terms of voltage then closed a "high" or "low" relay if the alveolar P_{CO_2} rose above or fell below preset limits of tolerance (3) These relays started a motor turning one way or the other depending on the polarity of the error detected (4) The motor slowly opened or closed a valve controlling the pressure excursions in the respirator and (5) As the pressure excursions in the respirator

were varied, the alveolar PCO_2 of the patient was altered appropriately until the error in ventilation was corrected. In this way a patient's alveolar PCO_2 was made to determine the pressure excursions

in his respirator much as arterial PCO_2 normally determines tidal volume. The device was used chiefly in efforts to correct gross chronic errors in ventilation.

PHARMACOLOGY AND THERAPEUTICS

(The following abstract was inadvertently omitted from the April 1953 issue of Clinical Research Proceedings. It should have appeared in the abstracts of the Midwestern Section, Chicago, November 1952.)

Toxic Effects of Placebo Administration. Stewart Wolf, Oklahoma City.

The need for careful placebo control in the evaluation of the effects of pharmacologic agents is well recognized; but there is less awareness of the need for similar control in the appraisal of toxic effects. In a carefully controlled experiment, Tolserol and lactose placebos of identical appearance were administered to 31 patients. The experimenters as well as the subjects were completely ignorant of what was being administered. Many of the patients had minor and equivocal complaints such as drowsiness and anorexia while they were taking both Tolserol and placebos. Only three patients had major reactions. One of them developed sudden overwhelming weakness, palpitation and nausea within

fifteen minutes of taking her tablets. Identical reactions occurred following placebos and Tolserol. A second patient developed a diffuse itchy erythematous maculopapular rash after 10 days of taking pills. A skin consultant considered the eruption to be typical of a dermatitis medicamentosa. After the pills were discontinued the eruption quickly cleared. The patient firmly refused to try another batch of pills. Later it was learned that she had developed the rash while taking placebos. A third patient within 10 minutes developed epigastric pain followed by watery diarrhea, urticaria and angioneurotic edema of lips. After 48 hours and again after 96 hours, a second and third trial of pills produced the same reaction. This patient was shifted to another batch. When the same reactions followed again, she was given no further pills. When the batches were finally identified at the conclusion of the experiments it was found that she had developed her severe reactions on both Tolserol and placebos.

Notices of Importance to Investigators

EDITORIAL

The Preparation of Research Abstracts

THE PRIMARY PURPOSE of a research abstract is to convey information. The President and the Section Chairmen use abstracts to decide what papers to put on the program. Other scientists read them to learn what has been investigated, and what was found. An abstract which does not tell these people what they need to know is useless.

The facts which a fellow scientist wants to know about an investigation are few, but definite. He wants to know who did it. He wants to know why the investigation was undertaken. He wants to know what methods were used, and what results were obtained. Finally, he wants to know what conclusions were drawn from these results. He wants this information to be complete, but concise. He wants it written in a language which he can understand. Since he is a scientist himself, he will not be impressed by needlessly abstruse technical jargon, but he may be confused and annoyed by it.

There are some rules about the form and content of abstracts which have become standard. Members who submit their abstracts are asked to follow them.

1. The title should consist of a brief statement of the nature of the investigation, followed by the names and addresses of the authors. It is understood that the first author is the "senior author," and the man who will present the paper, if it is selected for a program. Medical degrees, titles, and hospital appointments are omitted, but should be included in an accompanying letter. However, if the re-

search was made possible by a grant in aid, this fact may be included.

Sample: The Effect of Nitrite Ingestion upon the Ammonia Content of Hepatic Venous Blood. *John W. Throckmorton and Angus McBeth*. Sixth Medical Service, City Hospital, West Pines, Georgia, and Department of Medicine, Busby Medical School. (Aided by a grant from the Bullfinch Foundation.)

2. The body of the abstract should not be longer than 250 words, organized in the following manner:

- (a) A brief statement of the purpose of the study (one sentence).
- (b) A statement of the methods which were used.
- (c) A summary of the results which were obtained.
- (d) A statement of the conclusions which were reached.

It is not satisfactory to say "the results will be discussed," and it is equally unsatisfactory to go into great detail, to exhort, or to editorialize.

3. Abstracts should be submitted in *triplicate*, should be typed, and both title and body should be *double spaced*. The need for three copies is not merely a hangover from the editor's military service. One copy is used by the officers who select the program. One copy is edited and submitted to the printer. The third is retained in the files in case one of the other two is lost. By receiving the abstracts in standard form the Federation is able to save both time and expense in editing and retyping them before publication.

4. A covering letter should be sent along with each abstract submitted. This letter should give the mailing address of the senior author. This address is of great importance, because the senior author is the one who is notified if the paper is selected for presentation. If the senior author is in the armed services, he should indicate the person to whom letters should be sent, if he is suddenly called away to another post.

5. If none of the authors are members of the Federation, they must be sponsored by a member or a senior member. The man who

presents the paper need not be a member, but he must be under forty-one years of age.

Each year more and more abstracts are submitted to the meetings of the Federation, and each year the research behind them increases in complexity. That many men are making many studies, there can be no doubt; but what some of these men are doing and what they are finding out is occasionally a mystery. Their ability to uncover new information and to develop new ideas would be much more apparent if they improved their ability to communicate their knowledge to others.

Notices to Members

Forthcoming Meetings

MIDWESTERN SECTION: The annual meeting will take place on Thursday, October 29, 1953, in the Gold Room of the Congress Hotel, Chicago, Illinois. Abstracts should be submitted in *triplicate* not later than September 15, 1953, to Dr. Robert W. Schneider, Division of Medicine, Cleveland Clinic, 2020 East 93rd Street, Cleveland 6, Ohio.

EASTERN SECTION: The annual meeting will be held on Monday, January 4, 1954, from 9:00 A.M. to 5:00 P.M. in the Amphitheater of the Jimmy Fund Building of the Children's Medical Center in Boston, Massachusetts. Abstracts to be considered for presentation should be submitted in *triplicate* not later than November 10, 1953 to the Program Committee Chairman, Dr. Walter Judson, Evans Memorial Hospital, 65 East Newton Street, Boston, Massachusetts.

WESTERN SECTION: The annual meeting will be held on Thursday, January 28, 1954, in Portland, Oregon, in the auditorium of the University of Oregon Medical School. Headquarters of the convention will be the Old and New Heathman Hotels. Deadline for abstracts is November 15, 1953. They should be submitted in *triplicate* to Dr. Isidore S. Edelman, Secretary, University of California, Medical Office, San Francisco Hospital, Potrero and 22nd Streets, San Francisco, California.

SOUTHERN SECTION: The annual meeting will be held on January 29, 1954, at the Jung Hotel in New Orleans, in conjunction with the meeting of the Southern Society for Clinical Research. Abstract deadline is November 15, 1953. Abstracts should be submitted in *triplicate* to Dr. William Parson, University of Virginia, School of Medicine, Charlottesville, Virginia.

Changes of Address

The National Secretary should be notified at least 3 weeks prior to the date the change is to go into effect. Notice should include both the old and new address, and indicate whether the change is temporary or permanent. *Please do not fail to notify us; otherwise you will miss important announcements and will fail to receive CLINICAL RESEARCH PROCEEDINGS.*

Dues

Members who have failed to pay their dues will not receive the forthcoming issues of CLINICAL RESEARCH PROCEEDINGS. The American Federation for Clinical Research is a self-supporting organization, and cannot defray the expenses of publication without the contribution of its members. *Please pay your membership dues promptly.*

Proposed Amendment of the Constitution

At the annual meeting of the Federation, on May 2, 1942, the following resolution was submitted:

"That Article II, Section I of the Constitution be amended to read: There shall be two types of members: a) Members, and b) Senior members; that Article II, Section IIb, be omitted, and Section IIc be labeled IIb; and that Article VI, Section II d and Section IIIb and IIIc be omitted." (signed) Wm. H. Beierwaltes, Wm. Parson, John Hickam, Ivan L. Bennett, Jr. and Carleton B. Chapman.

This amendment will be discussed and voted upon at the next meeting of the Federation in May 1954.

Concerning "Style"

It is customary for a magazine to have a standard policy for abbreviations, punctuation, spelling, and the like—matters grouped under the general heading of "style." Mr. Duncan Mackintosh, the Senior Editor of Grune & Stratton, Inc., has had a great deal of experience in setting up the "style" for medical magazines, and has been very helpful in guiding our own policies in this matter. He has passed along the following information, which may be of interest to our contributors.

The use of standard abbreviations (RBC, for example) is desirable; when special or unusual abbreviations are employed, each should be followed by a parenthetical explanation the first time it is used. Numerals rather than words, should be used to indicate numbers. The per cent sign (%) is used. The PROCEEDINGS prefers such spellings as *technic*, *pipet*, and *gage*, rather than *technique*, *pipette*, and *gauge*. (We have not yet discovered what to do about *phthisis*.) The "al" ending is dropped from such words as *anatomic*, *biologic*, *hematologic*, *physiologic*, etc., but is retained in such words as *biochemical*. *Reticuloendothelial*, *gastro-*

intestinal, *postoperative*, and *nontransfusable* and similar terms are not hyphenated, whereas such words as *hypo-ovarian*, *post-traumatic*, and *non-nucleated* are.

These rules are, of course, arbitrary. They are not binding upon the contributors, and an abstract will be neither criticized nor rejected if the author spells out *three hundred and sixty-five*, or hyphenates *gastrointestinal*. However, if these items appear in a different form in the published text, we hope that he will understand that the change was made in the interest of uniformity and brevity. On the other hand, it is a matter of concern if the abstract is poorly typed. Please type on one side of the paper only, allow adequate margins, double-space all typewritten material, make carbons on regular white second sheets, rather than on "fimsies," and be sure that carbons are readable before submitting them.

In the matter of abstract headings, the journal may be examined for the proper amount of material, the order of items, and preferred style of punctuation, and capitalization. Please don't use all-capitals for abstract titles.

Special Notice

Persons knowing the present address of the following members are requested to notify the National Secretary-Treasurer, Dr. Lawrence E. Hinkle Jr., 525 East 65th Street, New York, 21, New York.

Theodore H. Aaron
Junior A. Abildskov
John B. Alsever
Eric Bell, Jr.
Theodore Bisland
Charles R. Blackburn
Robert N. Brown
Elmore C. Campbell
John W. Clairborne, Jr.
Robert C. Cogswell
George Cytroen
Arnold Danker
David P. Earle, Jr.
Archie Lee Edgar
William J. Fink
William Franklin
Herbert D. Friedlander
John K. Fulton
Donald S. Gair
Joseph Gaster
J. Golden
Charles M. Grossman
K. Albert Harden
Marian Grace Hayes

C. G. Holland
Lucius Brainerd Keels
Julius Richard Krevans
Richard L. Kendrick
W. Vernon Lee
G. M. Leiby
Herbert C. Lichtman
David Littman
Arthur H. Loomis
Robert H. Manheimer
William E. Martindale
J. P. Milthorp
John Caldwell Mithoefer
Augusto Mascarenhas
Walter H. Moursund, Jr.
Jacob Neber
Herbert A. Perkins
M. Pijoan
Walter C. Ralston
Alexander B. Procailo
William Ransohoff
Robert S. Reiss
John F. Renshaw
Hyman J. Rubitsky

Michel M. B. Saint-Paul
Arthur J. Samuels
David H. Solomon
Edward H. Scherr
Harold W. Schnaper
Carl F. Shaffer
John R. Sheehan
Howard D. Sirak
Kenneth McLane Smith
Ralph O. Smith
Rupard Glenn Smith
James L. Spencer, Jr.
Robert J. Stein
Daniel Steinberg
Samuel L. Stephenson, Jr.
John F. Sullivan
Frank Nelson Suma
Norman V. Treger
Samuel Waxler
Ferdinand Gerald Weisbrod
William C. Whitesides, Jr.
Abraham Wolbarsht
John J. Will
Leona B. Yeager
Albert S. Zdanis

1953 Membership Roster

of the

American Federation for Clinical Research

No Asterisk—Full Member

* Associate Member

** Senior Member

ALABAMA

Keehn Berry, Jr., 3228 Highland Dr., Birmingham 5.
 Louis L. Friedman, 1124 S. 20th St., Birmingham.
 Walter B. Frommeyer, 700 S. 19th St., Birmingham.
 Howard L. Holley, 620 S. 20th St., Birmingham 5.
 James B. McLester, ** 930 S. 20th St., Birmingham.
 G. W. Millett, ** V. A. Hospital, Birmingham.
 William B. Neal, Jr., Veterans Administration Hospital, Birmingham.
 Morris Schaeffer, ** U. S. Public Health Service, Box 61, Montgomery 1.
 Leon Smelo, ** 1005 S. 21st St., Birmingham.
 Tobias Stein, ** 3553 Southmont Dr., Montgomery 6.

ARKANSAS

Willis E. Brown, ** University Hospital, Little Rock.
 Edwin C. Jungck, Univ. of Ark., School of Medicine, Little Rock.
 Benjamin B. Wells, Univ. of Ark., School of Medicine, Little Rock.

CALIFORNIA†

Paul M. Aggeler, ** 655 Sutter St., San Francisco 2.
 Robert H. Alway, Stanford University, San Francisco.
 Harry E. Balch, ** Highland-Alameda County Hosp., Oakland.
 Donald C. Balfour, Jr., 3761 Stocker St., Los Angeles 8.
 Franz K. Bauer, Wadsworth Genl. Hosp., Los Angeles 25.
 Nathaniel I. Berlin, Donner Lab. of Med. Physics, U. of Calif., Berkeley 4.
 Howard R. Bierman, Lab. of Exptl. Oncology, Laguna Honda Home, San Francisco 16.
 Max W. Biggs, 1336 Brown Ave., Lafayette.
 Joy Bishop, * 2434 Haste St., Berkeley 4.
 Gerson R. Biskind, ** 450 Sutter St., San Francisco.

† See also Addenda, p. 143.

Lenore A. Boling, 3687 Greenacre Rd., Oakland.
 Ernest Bors, ** Birmingham V. A. Hosp., Van Nuys.
 E. Raymond Borun, 912 N. Whittier Dr., Beverly Hills.
 Warren L. Bostick, U. of C. Med. School, San Francisco 22.
 Robert I. Boyd, 960 E. Green St., Pasadena 1.
 Henry D. Brainerd, U. of C. Hosp. Med. Cntr., San Francisco 22.
 Ellen Brown, U. of C. Hosp. Med. Cntr., San Francisco 22.
 Henry B. Bruyn, 124 Windsor Ave., Berkeley 8.
 George Lloyd Calvy, ** M S T S West Pac. Area, % F.P.O., San Francisco.
 Espey F. Cannon, ** 2 West Fern Ave., Redlands.
 Boris Catz, 1322½ N. Harper, Los Angeles 46.
 Alfred W. Childs, 567 Ninth Ave., Menlo Park.
 Gilbert C. Cochran, * 128 Caper-ton Ave., Piedmont.
 Morris F. Collen, 4155 Walnut Blvd., Walnut Creek.
 Robert R. Commons, 436 N. Roxbury, Beverly Hills.
 Charles G. Craddock, Jr., U. of C. Med. Cntr., Los Angeles 24.
 Robert H. Crede, U. of C. Hosp., San Francisco 22.
 Harry A. Davis, ** 2007 Wilshire Blvd., Los Angeles 5.
 Quentin B. Deming, Stanford Med. School, Clay & Webster Sts., San Francisco 15.
 Loren T. DeWind, Crenshaw Med. Cntr., Stocker St., Los Angeles.
 Donald C. Dodds, 411 30th St., Oakland.
 Albert H. Domm, ** 5757 Wilshire Blvd., Los Angeles.
 Paul Doolan, U. S. Naval Hosp., Oakland.
 Edmund L. Dubois, 5720 Wilshire Blvd., Los Angeles 36.
 Isidor S. Edelman, San Fran. City & County Hosp., Potrero & 23rd Sts., San Francisco 10.
 Stephen R. Elek, 6423 Wilshire Blvd., Los Angeles 48.
 Maurice Eliaser, Jr., ** 655 Sutter St., San Francisco 2.

Henry Wood Elliott, U. of C. Med. School, San Francisco 22.
 Ephraim P. Engleman, ** 77 San Mateo Dr., San Mateo.
 Edward R. Evans, 1060 E. Green St., Pasadena.
 Eugene Farber, 536 Mason St., San Francisco.
 Seymour M. Farber, 516 Sutter St., San Francisco 2.
 Elliston Farrell, ** 117 E. Eighth St., Long Beach 13.
 John B. Field, U. of S. C., School of Med., Los Angeles 33.
 Nadine Foreman, Highland-Alameda County Hosp., 2701 14th Ave., Oakland 6.
 Richard D. Friedlander, ** 742 29th Ave., San Francisco 21.
 Albert Irving Gazin, 1301 Chorro, San Luis Obispo.
 Ernest Geiger, ** 3842 Monteith Dr., Los Angeles 43.
 Joseph E. Giansiracusa, U. of C. School of Med., San Francisco 22.
 W. W. Glas, * U. S. Army Hosp., Camp Roberts.
 Franz Rudolf Goetzl, 2622 Piedmont Ave., Berkeley 4.
 John William Gofman, U. of C. Div. of Med. Physics, Berkeley 4.
 Mervin J. Goldman, V. A. Hosp., Oakland 12.
 Ralph Goldman, 746 S. Genesee, Los Angeles 36.
 Gilbert S. Gordon, Jr., U. of C. Hosp., San Francisco.
 Paul O. Greeley, ** U. of S. C., Los Angeles 7.
 Byron E. Hall, ** 490 Post St., San Francisco 2.
 Joseph G. Hamilton, ** U. of C. Radiation Lab., Berkeley.
 Alexander Hatoff, 5744 Buena Vista Ave., Oakland 11.
 John Heintzelman, ** Navy 926, % FPO, San Francisco.
 E. Craig Heringman, 6351 Wilshire Blvd., Los Angeles 36.
 A. Gerson Hollander, ** V. A. Hosp., 13th & Harrison Sts., Oakland.
 James Hopper, Jr., ** U. of C. Hosp., San Francisco 22.
 Herbert N. Hultgren, Stanford U. School of Med., Clay & Webster Sts., San Francisco.

- James S. L. Jacobs, 2365 Via Anacapa, Palos Verdes Estates.
- John P. Jahn,* Fairmont Alameda County Hosp., 15400 Foothill Blvd., San Leandro.
- Ernest Jawetz, U. of C. Med. School, San Francisco 22.
- Hilliard J. Katz, 655 Sutter St., San Francisco.
- Nobuyuki Kawata,* San Fran. Hosp., 22nd & Potrero Sts., San Francisco 10.
- Keith H. Kelly, Lab. Expmntl. Oncology, Laguna Honda Home, San Francisco 16.
- C. Henry Kempe, Dept. of Ped., U. of C. Med. School, San Francisco.
- Lawrence W. Kinsell,** Highland-Alameda County Hosp., Oakland 6.
- Felix O. Kolb, U. of C. Med. Cntr., San Francisco 22.
- Benjamin Kondo, 3621 Brooklyn Ave., Los Angeles 63.
- Henry Kraus, Tokyo Army Hosp., 8050th AU APO 1052, % PM, San Francisco.
- Marcus A. Krupp, 300 Homer Ave., Palo Alto.
- George V. Kulchar,** 450 Sutter St., San Francisco 8.
- Robert D. Lange, Atomic Bomb Casualty Commission, APO 182, % PM, San Francisco.
- John H. Lawrence,** Donner Lab. Med. Physics, U. of C., Berkeley 4.
- John S. Lawrence,** U. of C. Med. Cntr., Los Angeles 24.
- Sanford H. Lawrence, 156½ Screenland Dr., Burbank.
- Sanford E. Leeds,** 3440 Washington St., San Francisco 18.
- Alan N. Leslie,** 525 N. Saltair Ave., Los Angeles 49.
- Leon Lewis,** 2380 Ellsworth St., Berkeley 4.
- Jonah G. Li, U. of C. Hosp., San Francisco 22.
- Stuart Lindsay, 802 Barneson Ave., San Mateo.
- Elizabeth Lowenhaupt,** 234 32nd Ave., San Francisco 21.
- Herbert I. McCoy, 6515 La Jolla Blvd., La Jolla.
- Charles E. McLennan,** Stanford U. Hosp., San Francisco 15.
- Harold Mankin, 3460 Richmond Blvd., Oakland 11.
- Sheldon Margen, 2380 Ellsworth St., Berkeley 4.
- M. Sydney Margolese,** 436 N. Roxbury Dr., Beverly Hills.
- Helen E. Martin,** 811 Bonita Dr., S. Pasadena.
- Serafeim P. Masouredis, 2941 Linden, Berkeley 5.
- Theodore B. Massell,** 544 S. Barrington Ave., Los Angeles 24.
- Willard M. Meininger, 2615 Eye St., Sacramento.
- Sherman M. Mellinkoff, 811 N. Foothill Rd., Beverly Hills.
- Stacy R. Mettler,** 40 Scenic Way, San Francisco.
- Morton A. Meyer, 2884 Telegraph Ave., Berkeley.
- Earl R. Miller,** 55 Ashbury Terr., San Francisco.
- T. M. Mizokoshi, % W. C. Moloney, Atomic Bomb Casualty Comm., APO 182, PM, San Francisco.
- William E. Molle, 1212½ S. La Cienga Blvd., Los Angeles 48.
- Henry D. Moon, U. of C. Med. School Path., San Francisco 22.
- Frank M. Morgan, 407 N. Central Ave., Glendale 3.
- Lester M. Morrison,** 6317 Wilshire Blvd., Los Angeles.
- Robert E. Morrison, 1009 Artson Ave., Rosemead.
- Grant Morrow, 909 Hyde St., San Francisco 9.
- Hurley L. Motley,** 2003 N. Serrano Ave., Los Angeles 27.
- Eli R. Movitt,** V. A. Hosp., 13th & Harrison Sts., Oakland 12.
- Theodore M. Meyers,* 652 N. El Camino Real, San Mateo.
- John R. Newkirk, 426 17th St., Oakland 12.
- H. W. Newman,** Stanford U. Hosp., San Francisco.
- Robert W. Oblath, Inst. for Med. Research, 4751 Fountain Ave., Los Angeles.
- Richard E. Ottoman,** U. of C. School of Med., 405 Hilgard Ave., Los Angeles 24.
- Nello Pace, U. of C. Div. of Physiol., Berkeley.
- Ernest W. Page,** U. of C. School of Med., San Francisco 22.
- Robert J. Parsons,** Highland Hosp., 2701 14th Ave., Oakland 6.
- John W. Partridge, 2633 Regent St., Berkeley 4.
- Donald W. Petit, 1200 N. State St., Los Angeles 33.
- Nicholas L. Petrakis, 800 Cedar Ave., San Bruno.
- Paul Pfeiffer, 1934 Rosecrest Dr., Oakland 2.
- Edward Phillips, 4036 Wilshire Blvd., Los Angeles 5.
- Frank T. Pierce, Jr., Donner Lab., U. of C., Berkeley 4.
- Phillip Raimondi, 517 Magnolia Ave., Piedmont 11.
- Lowell A. Rantz,** Stanford U. School of Med., San Francisco.
- Telfer B. Reynolds, Dept. of Med., U. of S. C., 1200 N. State St., Los Angeles 33.
- J. Alfred Rider, U. of C. Hosp., San Francisco 22.
- H. Schuyler Robertson, Jr., 2191 El Camino Real, San Mateo.
- Saul J. Robinson,** 2215 Post St., San Francisco 15.
- Milton L. Rosenberg, Stanford U. Hosps., Clay & Webster Sts., San Francisco 15.
- Harold Rosenblum,** 450 Sutter St., San Francisco.
- David A. Rytand,** Stanford U. Hosp., San Francisco 15.
- Joseph F. Sadusk, Jr.,** 2930 McClure St., Oakland 9.
- Arthur Selzer,** 450 Sutter St., San Francisco 8.
- Benjamin Simkin, 6228 Wilshire Blvd., Los Angeles 48.
- Robert F. Skeels, Shelton Clinic, 921 Westwood Blvd., Los Angeles 24.
- Charles E. Smith,** School of Pub. Health, U. of C., Berkeley 4.
- Stephen Smith, III, Las Encinas, Pasadena 10.
- Leopold J. Snyder,* 1212 Security Bank Bldg., Fresno.
- Maurice Sokolow,** 3452 Jackson St., San Francisco 18.
- David H. Solomon, 525 N. Rexford Dr., Beverly Hills.
- Theodore H. Spaet, Stanford U. School of Med., Clay & Webster Sts., San Francisco.
- Reinhard S. Speck, U. of C. School of Med., San Francisco 22.
- Paul Starr,** 1199 Lida St., Pasadena 2.
- Lloyd Stirrett, 11333 Kiel St., Los Angeles 49.
- Carlyle F. Stout, 1930 Wilshire Blvd., Los Angeles 57.
- Louis A. Strait,** 204 Grand View Ave., San Francisco 14.
- Virginia M. Stuermer, 4422 Burns Ave., Hollywood 29.
- J. W. Stutzman, 8480 Beverly Blvd., Los Angeles.
- Norman J. Sweet, U. of C. Hosp., San Francisco 22.
- James T. Taguchi, 21st Evac. Hosp., APO 59, % PM, San Francisco.
- G. Douglas Talbott, 427 38th Ave., San Francisco.
- H. Grant Taylor,** A.B.C.C., APO 182, % PM, San Francisco.
- James H. Thompson, 384 Post St., San Francisco 8.
- Walter S. Thompson, Jr.,* 1136 W. 6th St., Los Angeles 14.
- Frank W. Van Kirk, Jr.,* 3875 Wilshire Blvd., Los Angeles 5.
- Charles J. Wallace,* 2615 Eye St., Sacramento 16.
- Ralph O. Wallerstein, 2000 Van Ness Ave., San Francisco 9.
- George F. Warner, 655 Sutter St., San Francisco 2.
- Edgar Wayburn,** 490 Post St., San Francisco.
- Ralph W. Weilerstein,** U. S. Food & Drug Admin., 512 Federal Office Bldg., San Francisco.
- Howard J. Weinberger, 6363 Wilshire Blvd., Los Angeles 48.
- Harry A. Weiss, 1079 Devonshire Dr., San Diego 7.
- Herbert A. Weitzner,** 605 Curtis St., Albany.
- Henry M. Weyrauch,** Stanford

U. School of Med., 2398 Sacramento St., San Francisco 15.
Laurens P. White, 149 Castro St., San Francisco.
Sidney G. White, 15911 Leadwell St., Van Nuys.
Francis N. Wilson, 3022 E. 14th St., Oakland.
Travis Winsor, 3875 Wilshire Blvd., Los Angeles 5.
Paul Yamauchi, 1619 Berkeley Way, Berkeley 3.
Eric Theodor Yuhl, 1486 Glendon Ave., Los Angeles 24.
Willard J. Zinn, 828 N. 2nd St., Alhambra.
Hans H. Zinsser, 127 N. Madison Ave., Pasadena 1.

COLORADO†

Martin M. Alexander, 709 Republic Bldg., Denver.
Leighton L. Anderson,** 4200 E. 9th Ave., Denver.
Oscar Balchum, Cardio-Pulmonary Lab., National Jewish Hosp., Denver 6.
James C. Bell, 4200 E. 9th Ave., Denver.
Willis L. Bennett, 736 Metropolitan Bldg., Denver 2.
Robert F. Berris, 330 Metropolitan Bldg., Denver.
John W. Berry, 595 Gilpin, Denver.
S. Gilbert Blount, Jr., 4200 E. 9th Ave., Denver.
Neal S. Bricker,* 1550 Glencoe, Denver.
Paul D. Bruns, U. of Colorado, School of Med., Denver 7.
Dumont Clark,** 1731 Gilpin St., Denver.
Henry Clay Cleveland, 1438 Niagara St., Denver.
William B. Condon,** 1612 Tremont St., Denver 2.
Autrey R. Croke,* 23 E. Pikes Peak Ave., Colorado Springs.
Douglas Deeds,** 700 Metropolitan Bldg., Denver.
Sidney H. Dressler,** 4633 E. Dartmouth Ave., Denver.
Reginald H. Fitz,* Denver General Hosp., 6th & Bannock, Denver.
Martin J. FitzPatrick, Fitzsimons Army Hosp., Denver 8.
Goffredo G. Gensini,* 1710 E. 22nd Ave., Denver.
John H. Githens, 4200 E. 9th Ave., Denver.
Eli S. Goldensohn, U. of Colorado Med. School, 4200 E. 9th St., Denver.
Lloyd J. Gregory, 811 Ursula St., Denver 8.
Russell W. Hibbert, Jr., 821½ Ninth St., Greeley.
William A. Hines, 1801 Williams, Denver.
Joseph H. Holmes,** U. of Colo-

rado Med. Cntr., 4200 E. 9th Ave., Denver 7.
Elston R. Huffman, V. A. Hosp., Denver.
Frederic J. Hughes, Jr., Fitzsimons Army Hosp., Denver 8.
Melvin A. Johnson,* 1776 Vine St., Denver.
Frank T. Joyce,** 1059 Newport St., Denver.
A. J. Kauvar, 3705 E. Colfax, Denver.
Fred Kern, Jr., Denver General Hosp., Denver.
Ben M. Leeper,* 475 Garfield St., Denver.
Hope Lowry, 4200 E. Ninth Ave., Denver.
Malcolm C. McCord, Colorado General Hosp., 4200 E. Ninth Ave., Denver 20.
John G. McDonald, 2750 Broadway, Boulder.
Frank B. McGlone, 801 Detroit St., Denver.
Edward S. Miller, Med. Cntr. Associates, 3705 E. Colfax Ave., Denver 6.
Rollen W. Moody,* 612 Harrison St., Denver 6.
Rosalie Neligh, U. of Colorado, Boulder.
James C. Owens, U. of Colorado Med. Cntr., 4200 E. Ninth Ave., Denver 7.
Mordant E. Peck, 3365 Ash St., Denver 7.
James A. Philpott, Jr., 434 Metropolitan Bldg., Denver.
Forrest W. Pitts, Fitzsimons Army Hosp., Denver 8.
Elmer B. Pratt,** 781 Kearney St., Denver.
Frederick J. Rachiele, 1055 Clermont St., Denver.
Abe Ravin,** 425 Republic Bldg., Denver.
Howard T. Robertson, 3705 E. Colfax, Denver 6.
James H. Sands, 735 Seranton St., Aurora.
E. Paul Sheridan, 1776 Vine, Denver.
David W. Sinton, 1938 N. Wood Ave., Colorado Springs.
N. Balfour Slonim, 2374 Grape St., Denver.
Charley J. Smyth,** Dept. of Med., U. of Colorado, 4200 E. 9th St., Denver 7.
William W. Stead, Fitzsimons Army Hosp., Denver.
Bill D. Stewart, 755 Birch, Denver.
Oliver G. Stonington, 950 Lafayette St., Denver.
Henry Swan, U. of Colo. School of Med., Denver.
Milton N. Towbin, 1820 Locust St., Denver.
J. A. Wier, Officers Mail, Fitzsimons Army Hosp., Denver 8.
George Dawley Wilcox, III,* 712 Glencoe St., Denver.
Thomas A. Witten, % V. A. Hosp., Denver.

CONNECTICUT

Frank K. Abbot, 163 Grove St., Waterbury.
Margaret J. Albrink, Yale Univ. School of Med., New Haven.
Thomas T. Amatruda, Jr., Grace-New Haven Community Hosp., New Haven.
John F. Beakey, 703 Asylum Ave., Hartford.
Paul B. Beeson,** Yale Univ. School of Med., 789 Howard Ave., New Haven 11.
Ivan L. Bennett, Jr., Yale Univ. School of Med., New Haven.
Philip K. Bondy, 789 Howard Ave., New Haven.
Joseph H. Burchenal, Juniper Hill Rd., Noroton.
David H. Clement,** 240 Bradley St., New Haven 10.
Harold O. Conn,* Yale Univ. School of Med., New Haven.
Allan J. Erslev, Maple Road, Stony Creek.
Chester W. Fairlie,* Hosp. for Chronic Illness, Rocky Hill.
Alvan R. Feinstein, Grace-New Haven Community Hosp., New Haven.
Stephen Fleck, Yale Univ. School of Med., 333 Cedar Street, New Haven.
Lawrence R. Freedman, 943 Elm St., New Haven.
Gilbert H. Glaser, Yale Univ. School of Med., New Haven.
Allan V. N. Goodyer, Yale Univ. School of Med., New Haven.
Robert S. Gordon, Grace-New Haven Community Hosp., New Haven.
Frank D. Gray, Jr., Yale Univ. School of Med., New Haven.
Frieda G. Gray, Yale Univ. School of Med., New Haven.
Robert H. Green,** Yale Univ. School of Med., New Haven 11.
Mark A. Hayes, Yale Univ. School of Med., 489 Howard St., New Haven 4.
John H. Heller, Yale Univ. School of Med., New Haven.
Kenneth G. Johnson,* Grace-New Haven Community Hosp., New Haven.
Gerald Klatsin,** Yale Univ. School of Med., New Haven 11.
Charles R. Kleeman, Yale Univ. School of Med., New Haven.
Sung Jui Liao, Yale Univ. School of Med., New Haven.
Seymour R. Lipsky,* 20 Edgewood Ave., New Haven.
Robert G. Petersdorf, Grace-New Haven Community Hosp., New Haven.
Milton E. Rubini,* Yale Univ. School of Med., New Haven.
Sylvester J. Ryan,* Grace-New Haven Community Hosp., New Haven.
William B. Scoville,** 85 Jefferson St., Hartford 6.

† See also Addenda, p. 143.

Paul H. Seton, 70 Central Ave., New Haven.
 Henry K. Silver, Yale Univ. School of Med., 789 Howard Ave., New Haven 4.
 Joseph E. Sokal, Yale Univ. School of Med., New Haven.
 Kenneth Sterling, Yale Univ. School of Med., 789 Howard Ave., New Haven.
 William E. Swift,* 10 Lincoln St., New Haven 10.
 Willem F. Van Eck, Yale Univ. School of Med., New Haven.
 Robert R. Wagner, Yale Univ. School of Med., 333 Cedar St., New Haven 11.
 Benjamin White,** 85 Jefferson St., Hartford 6.
 William W. Winternitz, Yale Univ. School of Med., New Haven.

DELAWARE

A. Henry Claggett, Jr.,** V. A. Hosp., Wilmington.
 Robert L. Dewees,* 1005 Jefferson St., Wilmington.
 Joseph J. Kristan,* 88 University Ave., New Castle.
 Leonard P. Lang, 1009 Delaware Ave., Wilmington 7.
 Richard A. Neubauer, Memorial Hosp., Wilmington.
 Armine T. Wilson,** Alfred I. du Pont Inst. of The Nemours Foundation, Wilmington 99.

DISTRICT OF COLUMBIA†

Louis K. Alpert,** V. A. Hosp., 2650 Wisconsin Ave., N.W., Washington 7.
 Jeanne C. Bateman,** 1229 37th St., N.W., Washington 7.
 Edward J. Beattie, Jr., George Washington Univ. Med. School, Washington.
 Virginia P. Beelar,* 5715 Massachusetts Ave., Washington 16.
 Irving B. Brick, Georgetown Univ. Hosp., Washington 7.
 Gus G. Casten, Army Med. Serv. Grad. School, Army Medical Center, Washington 12.
 Nicholas J. Cotsonas, Jr., Gallinger Municipal Hosp., Washington 3.
 Arthur Dick,** 1614 Rhode Island Ave., Washington 6.
 Henry D. Ecker,* 3309 Highland Place, N.W., Washington.
 Clayton B. Ethridge,** 915 19th St., N.W., Washington 6.
 John Evans, George Washington Univ. Hosp., 23rd & Pennsylvania Ave., Washington.
 Frank A. Finnerty, Jr., Gallinger Hosp., Washington.
 Richard H. Fischer, 915 19th St., N.W., #1000, Washington.
 Robert A. Fishman, Army Med. Serv. Grad. School, Walter Reed Army Med. Cntr., Washington 12.

† See also Addenda, p. 143.

Edward Freis, V. A. Hosp., 2650 Wisconsin Ave., N.W., Washington 7.
 Adolph Friedman, Farragut Med. Bldg., 900 17th St., N.W., Washington 6.
 John F. Gillespie, 2222 Eye St., N.W., Washington.
 Margaret E. Grigsby, Howard Univ. School of Med., Washington.
 Edward H. Hale, 3729 Jay St., N.E., Apt. 5, Washington 19.
 Charles R. L. Halley,** 915 19th St., N.W., Washington 6.
 W. Proctor Harvey, Georgetown Univ. Hosp., Washington 7.
 Harry Helmann,** Industrial Hygiene Div., Public Health Serv., Washington 25.
 Harold Hirsh, 2945 Brandywine St., N.W., Washington 8.
 Harry Horstman, Jr.,* Walter Reed Army Hosp., Washington 12.
 William L. Howell,** 1801 K St., N.W., Washington 6.
 Charles A. Hufnagel, Georgetown Univ. Hosp., 3900 Reservoir Rd., Washington.
 Harold Jeghers,** Georgetown Univ. Hosp., 3800 Reservoir Rd., N.W., Washington 7.
 John B. Johnson,** Howard Univ. School of Med., Washington.
 Robert T. Kelley, 3132 16th St., N.W., Washington 9.
 Althea Kessler,* 5060 MacArthur Blvd., N.W., Washington 16.
 Albert D. Kistin,** 2111 Bancroft Pl., N.W., Washington 8.
 Calvin T. Klopp, 1339 H Street, N.W., Washington.
 Laurence H. Kyle, Georgetown Univ. Hosp., Washington 7.
 Maurice Landy, Immunology Div., AMDR & GS, Washington 12.
 Benjamin Manchester,** 1701 Varum St., N.W., Washington 11.
 Thomas W. Mattingly,** Walter Reed Army Hosp., Washington 12.
 Maurice Mensh,* 1730 Eye St., Washington 6.
 William R. Merchant, 2650 Wisconsin Ave., N.W., Washington 7.
 William H. Meroney, III, Walter Reed Army Med. Cntr., Washington 12.
 R. Bretney Miller,** 1834 Eye St., N.W., Washington 6.
 James M. Moss, 1835 Eye St., N.W., Washington 6.
 Arno G. Motulsky, Walter Reed Army Med. Cntr., Washington.
 Loren F. Parmley, Jr., Walter Reed Army Med. Cntr., Washington 12.
 Edward A. Partenope,* 4934 Wisconsin Ave., N.W., Washington.
 Milton H. Paul, Walter Reed Army Med. Cntr., Washington 12.

Elbert T. Phelps, Georgetown Univ. Hosp., Washington 7.
 Irvin C. Plough, Walter Reed Army Med. Cntr., Washington 12.
 Andrew G. Prandoni,** 1150 Connecticut Ave., N.W., Washington.
 Charles E. Rath, Georgetown Univ. Hosp., Washington 13.
 John A. Reed,** 1720 Connecticut Ave., N.W., Washington 9.
 Jack J. Rheingold, 1601 Argonne Place, N.W., Washington 7.
 Roy Elliot Ritts, Jr.,* 2701 32nd St., S.E., Washington 20.
 Monroe J. Romansky,** George Washington Univ. Hosp., 910 23rd St., N.W., Washington 7.
 John C. Rose, Georgetown Univ. Hosp., Washington.
 John B. Ross,* 1150 Connecticut Ave., N.W., Washington 16.
 Sidney Ross, 5601 Utah Ave., N.W., Washington.
 Victor M. Sborov, Walter Reed Army Med. Cntr., Washington 12.
 George E. Schreiner, 2025 Eye St., N.W., Washington 6.
 Roland B. Scott,** 1114 Girard St., N.W., Washington.
 Frederick Stohlman, Jr.,* Georgetown Univ. Hosp., Washington.
 Ernest G. Theilen, A.M.S.G.S., Army Med. Cntr., Washington 12.
 Lawrence Thomas,* 900 17th St., N.W., Washington 6.
 Riley Thomas,** 1326 Girard St., N.W., Washington.
 Charles W. Thompson,* 1714 N Street, N.W., Washington 6.
 J. Lawn Thompson, Jr.,** 1714 N St., N.W., Washington.
 Eugene J. Towbin, Walter Reed Army Med. Cntr., Washington 12.
 A. Earl Vivino, 3800 Reservoir Rd., N.W., Washington 7.
 Jacob J. Weinstein,** 900 17th Street, N.W., Washington.
 Arnold H. Williams, Walter Reed Army Med. Cntr., Washington 12.
 Irving W. Winik, 5415 Connecticut Ave., N.W., Washington 15.
 Charles S. Wise, George Washington Univ. Hosp., 901 23rd St., Washington 7.

FLORIDA

Barkley Beidleman,* The Medical Center, 24 W. Chase St., Pensacola.
 Martin S. Belle, 1431 N. Bayshore Dr., Miami 36.
 Clarence Bernstein,** 740 Magnolia Ave., Orlando.
 Robert Boucek, 515 N.E. 15th St., Miami.
 Everett M. Bowser, 100 S.W. 53th Ave., Miami.
 Chester Cassel, Huntington Bldg., Miami.

C. Frank Chunn, 442 W. Lafayette Ave., Tampa.

Morris M. Dick,** 3301 S.W. 18th St., Miami.

William J. East,** V. A. Hosp., Lake City.

Willis F. Evans,** Warrington, Sidney Grau, 2169 22nd Ave., N., St. Petersburg.

Dale Groom, 1342 Du Pont Bldg., Miami.

Warren J. Hunzicker, Naval School Aviation Med., Pensacola.

Emil M. Isberg, 5145 Lakeview Dr., Miami Beach.

Nathaniel Jones,** 1804 Thacker Ave., Jacksonville 2.

Sherman R. Kaplan, 541 Lincoln Rd., Miami Beach.

Solomon D. Klotz, 1665 Berkshire Ave., Winter Park.

Victor H. Kugel,** 1700 Meridian Ave., Miami Beach 39.

Edward Larson,** V.A. Hospital, Coral Gables 34.

Warren Lindau,* 3725 S.W. 60th Court, Miami.

Bertrand E. Lowenstein, R.F.D. 2, Box 207, Miami.

Donald F. Marion,** 635 Palermo Ave., Coral Gables.

Samuel Myerson,** Bay Pines Veterans' Hosp., Bay Pine.

Benjamin G. Oren, 1431 N. Bayshore Dr., Miami.

Arthur H. Reynolds,** 1401 Jungle Ave., St. Petersburg 6.

Maurice Rich, 1431 N. Bayshore Dr., Miami.

Jack A. Rudolph,** 1310 100th St., Bay Harbor Is., Miami Beach.

John M. Rumball,** V. A. Hospital, Coral Gables.

Louis M. Sales,** 1204 Lebaron Ave., Jacksonville.

Murray Sanders,** Univ. of Miami, Box 1438, South Miami.

Milton S. Saslaw,** National Children's Cardiac Home, 4250 W. Flagler St., Miami.

Peritz Scheinberg, V. A. Hosp., Coral Gables.

Benjamin L. Steinberg,** V. A. Hospital, Lake City.

Franz H. Stewart,** 803 Du Pont Bldg., Miami.

Sidney Storch, 2232 Larchmont Rd., Jacksonville.

Mark Streitfeld, National Children's Cardiac Hosp., 4250 W. Flagler St., Miami 34.

Paul N. Unger, 420 Lincoln Rd., Miami Beach.

E. Coleman Whitaker,* V. A. Hosp. Lake City.

Edward F. Zimmerman,** V. A. Hospital, Anastasia Ave., Coral Gables.

GEORGIA

Osler A. Abbott, Emory Univ. Hosp., Atlanta.

Elbert B. Agnor,** Medical Arts Bldg., Atlanta.

Walter M. Bartlett,** 125 Michigan Ave., Decatur.

Joseph G. Bohorofoush,** V. A. Hosp. (Annex), Augusta.

Emmett S. Brannon,** McCall Hosp., Rome.

H. Eugene Brown, 21 Eighth Street, N.E., Atlanta.

E. Napier Burson, Jr.,* Lawson V. A. Hosp., Chamblee.

John F. Busch,** 310 McDonald, Marietta.

Thomas S. Claiborne,** 384 Peachtree St., Atlanta.

Robert P. Coggins, Univ. Hosp., Augusta.

Gerald R. Cooper, Communicable Disease Cntr., Box 185, Chamblee.

Martin M. Cummings, V. A. Hosp., Atlanta.

Albert M. Deal,* Box 268, Statesboro.

William L. Dobes, 478 Peachtree St., N.E., Atlanta.

William B. Fackler, Jr.,* 304 Church St., La Grange.

George L. Forbes, Jr.,* 3282 E. Roxboro Rd. N.E., Atlanta.

Milton H. Freedman, 21 8th St., N.E., Atlanta.

Abner Golden, Emory Univ. Hosp., Atlanta.

Paul H. Guilfoil,* 128 Mockingbird Lane, Decatur.

Albert Heyman, Grady Hosp., Atlanta 3.

J. H. Hilsman,* 104 Ponce De Leon Ave., N.E., Atlanta.

William A. Hopkins, 835 W. Ponce de Leon Ave., Decatur.

John W. Hurst, 2857 N. Hills Dr., N.E., Atlanta.

Alexander D. Langmuir,** U. S. Public Health Serv., Atlanta 5.

Clarence L. Laws,** 384 Peachtree St., Atlanta.

Bernard S. Lipman,* Emory Univ. Hosp., Atlanta.

R. Bruce Logue,** Emory Univ. Hosp., Atlanta.

Charles L. Lynch, Box 1516, Ft. Benning.

A. Park McGinty,** 762 Cypress St., N.E., Atlanta.

Emanuel E. Mandel,** 36 Butler St., S.E., Atlanta 3.

Arthur J. Merrill,** 35 4th St., N.E., Atlanta.

Max Michael, Jr., Lawson V. A. Hosp., Chamblee.

William R. Minnich,** 1010 Medical Arts Bldg., Atlanta.

James LeRoy Morrison, Emory Univ., Atlanta.

Glenn E. Mortimore, Grady Memorial Hosp., Atlanta.

Sidney Olansky, V. D. Lab., Box 185, Chamblee.

John H. Peters, V. A. Hosp., Atlanta.

Arthur P. Richardson,** Emory Univ. Med. School, Atlanta.

C. Purcell Roberts,** 762 Cypress, N.E., Atlanta.

Spalding Schroder,* Emory Univ. Hosp., Atlanta.

Joseph A. Schwartz,** V. A. Hospital, 5998 Peachtree Rd., N.E., Atlanta.

Walter H. Sheldon,** 36 Butler St., S.E., Atlanta 3.

Carter Smith,** 1210 Medical Arts Bldg., Atlanta.

Leland E. Starr,** 2005 Palifox Dr., N.E., Atlanta.

Hymen B. Stillerman, 26 Linden Ave., N.E., Atlanta.

C. F. Stone,** 42 W. Brookhaven Dr., N.E., Atlanta.

Lloyd F. Timberlake,* 670 Longwood Drive, N.W., Atlanta.

Irvin H. Trinchler,** 1250 University Dr., N.E., Atlanta.

George L. Walker, Jr.,** 319 S. 8th St., Griffin.

Robert L. Whipple, Jr., 384 Peachtree St., N.E., Atlanta.

Bernard P. Wolff,** 911 Medical Arts Bldg., Atlanta.

Edgar Woody, Jr., 1210 Medical Arts Bldg., Atlanta.

IDAHO†

Maurice M. Burkholder, 401 Idaho St., Boise.

Roy C. Crosby, 3709 Overland Rd., Boise.

Bernard L. Kreilkamp, 168 Pierce St., Twin Falls.

Paul F. Miner,** 11 Eastman Bldg., Boise City.

Samuel M. Poindexter,** 105 N. 8th St., Boise.

Burton R. Stein, 307 St. Johns Way, Lewiston.

Glenn Q. Voyles, 1515 Addison Ave., E., Twin Falls.

ILLINOIS

Stuart Abel, 700 Michigan Ave., Chicago 11.

Donald G. Anderson, 535 N. Dearborn St., Chicago.

Gerald H. Becker, 16 N. Mayfield Ave., Chicago 44.

Gerald Berenson, 5529 University, Chicago 37.

Delbert M. Bergenstal, Dept. of Med., Univ. of Chi., 950 E. 59th St., Chicago 37.

Lionel M. Bernstein, Univ. of Ill. College of Med., 1853 W. Polk St., Chicago.

William R. Best, 1853 West Polk St., Chicago.

William F. Bethard, Dept. of Med., Univ. of Chi., Chicago 37.

Ben B. Blivaiss, Chicago Med. School, 710 S. Wolcott Ave., Chicago 12.

David B. Carmichael, Jr., U. S. Naval Hosp., Great Lakes.

Robert W. Carton, 5 S. Wabash Ave., Chicago 3.

Melvin M. Chertack, 6920 N. McAlpin, Chicago.

† See also Addenda, p. 143.

- Harold W. Christy,** 720 N. Michigan Ave., Chicago.
 T. Howard Clarke,** 925 N. Michigan Ave., Chicago.
 Charles B. Clayman, 950 E. 59th St., Chicago 37.
 Harley E. Cluxton, Jr., 303 E. Chicago Ave., Chicago 11.
 Clarence Cohn,** Michael Reese Hosp., Chicago.
 George M. Cummins, Jr., 1039 Pine St., Winnetka.
 Ralph E. Dolkart, 670 N. Michigan Ave., Chicago.
 Harry F. Dowling,** Univ. of Ill. College of Med., Chicago 12.
 Frank R. Elliott, 874 Green Bay Rd., Winnetka.
 Shirl O. Evans, Jr., Univ. of Chicago Clinics, 950 E. 59th St., Chicago 37.
 Inga L. Faller, Box 2585, Hines.
 Edwin Feldman,* Ill. Masonic Hosp., 836 W. Wellington Ave., Chicago 14.
 Oscar Felsenfeld,** 4804 Quincy St., Chicago 44.
 Piero Pio Foa,** Chicago Med. School, 710 S. Wolcott Ave., Chicago.
 Sanford A. Franzblau, 106 Keystone Ave., River Forest.
 Nicholas W. Fugo, Chi. Lying-In Hosp., Univ. of Chi., Chicago 37.
 Robert P. Gilbert, Cook County Hosp., Chicago 12.
 A. Robert Goldfarb,** Chicago Med. School, 710 S. Wolcott Ave., Chicago.
 Robert L. Grissom, Univ. of Ill. College of Med., 1853 W. Polk St., Chicago.
 Herbert J. Grossman,* Univ. of Ill. College of Med., 1819 W. Polk St., Chicago 12.
 Harry S. Guterman, Michael Reese Hosp., Chicago 16.
 Buford Hall,* Ill. Rsrch. & Educ. Hosps., 1853 W. Polk St., Chicago 12.
 William H. Harridge, Ill. Rsrch. & Educ. Hosps., 1819 W. Polk St., Chicago 12.
 George A. Hellmuth,** 31 N. State St., Chicago 2.
 Marvin M. Hirsch, Univ. of Ill. College of Med., 1857 W. Polk St., Chicago 12.
 Erwin Huston,* 102 E. Chestnut St., Chicago.
 George G. Jackson, 120 Mohawk Dr., Clarendon Hills.
 Hushang Javid,* 4960 Marine Dr., Chicago.
 Richard J. Jones, 950 E. 59th St., Chicago 37.
 Robert M. Kark,** Univ. of Ill. College of Med., 1853 W. Polk St., Chicago 12.
 Donald L. Kessler,* 2726 Thayer, Evanston.
 Arthur P. Klotz, 950 E. 59th St., Chicago 37.
 Harold Koenig, Chicago Med. School, 710 S. Wolcott St., Chicago 12.
 Walter J. Kuhl, Jr., Med. Nutrition Lab., 1819 W. Pershing Rd., Chicago 9.
 Calvin R. Lantz, Jr.,* 1355 N. Hudson, Chicago 10.
 Jules H. Last, 668 Park Ave., Highland Park.
 Harold Laufman, 25 E. Washington St., Chicago.
 Mark Lepper, 327 Hampton Pl., Hinsdale.
 Jack J. Lewis, Dept. of Med., Univ. of Chi., Chicago 37.
 Howard A. Lindberg,** 670 N. Michigan Ave., Chicago 11.
 Morris A. Lipton, Dept. of Med., Univ. of Chi. Clinics, 950 E. 59th St., Chicago 37.
 Armand Littman, 244 E. Pearson St., Chicago 11.
 John Louis,* 10721 S. Hoyne Ave., Chicago 43.
 Aldo A. Luisada,** Chicago Med. School, 2755 W. 15th St., Chicago 8.
 Gerald O. McDonald, 1500 Lake Shore Dr., Chicago.
 Ernest G. McEwen,** 2672 Orrington Ave., Evanston.
 William P. McKeever, % G. D. Searle & Co., Box 5110, Chicago 80.
 Walter G. Maddock,** 250 E. Superior St., Chicago 11.
 William Mandel, Univ. of Ill. College of Med., Chicago.
 Francis R. Manlove, % A.M.A., 535 N. Dearborn St., Chicago.
 Carl J. Marienfeld, Univ. of Ill. Dept. of Ped., 1819 W. Polk St., Chicago.
 Harold L. Method,* 163 E. Walton Pl., Chicago 11.
 Hugo C. Moeller, Billings Hosp., 950 E. 59th St., Chicago.
 Robert C. Murphy, 1640 Jersey, Quincy.
 L. A. Nalefski,** Northwestern Univ. School of Med., Chicago 11.
 William R. O'Connor, 4823 W. Balmoral Ave., Chicago 30.
 Lester D. Odell,** Chicago Lying-In Hosp., Chicago 37.
 Stanley W. Olson, Univ. of Ill. College of Med., 1853 E. Polk St., Chicago.
 Luke Pascal, 40 E. 118th Pl., Chicago.
 Jerome Paul, 8 S. Michigan Ave., Chicago 3.
 Raymond Pearson, 1925 Hamilton Ct., Springfield.
 David T. Petty, Box 203, Hines.
 Ruth Pick, Michael Reese Hosp., 29th & Ellis Ave., Chicago 16.
 Sophie J. Presley, 4753 N. Broadway, Chicago 40.
 Frederick W. Preston, 952 N. Michigan Ave., Chicago 11.
 Theodore N. Pullman, Univ. of Chi. Clinics, 950 E. 59th St., Chicago 37.
 Theron G. Randolph,** 700 N. Michigan Ave., Chicago 11.
 Sigwin B. Raska,** 545 Graceland Ave., Des Plaines.
 Alexander P. Remenchik, 6511 S. Aberdeen St., Chicago 21.
 Simon Rodbard,** Michael Reese Hosp., Chicago 16.
 Cyrus E. Rubin, Dept. of Med., Univ. of Chi., Chicago 37.
 Robert B. Rutherford, 621 Jefferson Bldg., Peoria.
 Max S. Sadove, Univ. of Ill., 1819 W. Polk St., Chicago 12.
 George A. Saxton, Jr., Univ. of Ill. College of Med., S. Wood St., Chicago 12.
 James A. Schoenberger, 355 Windsor Ave., Glen Ellyn.
 Steven O. Schwartz,** 55 E. Washington St., Chicago 2.
 Irving Siegel,** 5054 N. St. Louis Ave., Chicago 25.
 Earl N. Silber, Michael Reese Hosp., 29th & Ellis Ave., Chicago 16.
 Karl Singer,** Michael Reese Hosp., 29th & Ellis Ave., Chicago.
 Harold W. Spies, 3026 S. California St., Chicago 8.
 Harold M. Spinka, 6132 S. Kedzie Ave., Chicago 29.
 Jeremiah Stamler, 5414 Ingleside Ave., Chicago.
 Irving F. Stein, Jr., 25 E. Washington St., Chicago 2.
 Robert C. Stepto, 6636 Minerva Ave., Chicago 37.
 Kurt Stern,** 2750 W. 15th Pl., Chicago 8.
 Robert T. Stormont, A.M.A., 535 N. Dearborn St., Chicago 10.
 George C. Sutton, 636 Church St., Evanston.
 Peter J. Talso, Mercy Hosp., 2537 S. Prairie Ave., Chicago 17.
 E. Clinton Texter, Jr., 700 N. Michigan Ave., Chicago 11.
 Theodore R. Van Dellen,** 303 E. Chicago Ave., Chicago 11.
 John W. Vester,* Med. Nutrition Lab., 1819 W. Pershing Rd., Chicago.
 Harry A. Waisman,* Univ. of Ill. College of Med., 1819 W. Polk St., Chicago 12.
 Maurice H. Wald,** 522 Green Bay Rd., Winnetka.
 Eugene L. Walsh,** 1130 Raleigh Rd., Glenview.
 Harry A. Warren,** 530 Alliance Life Bldg., Peoria.
 William H. Wehrmacher, 670 N. Michigan Ave., Chicago.
 Henry E. Wilson, Jr.,** 250 E. Superior St., Chicago 11.
 Irwin C. Winter,** 712 Chatham Rd., Glenview.
 Richard J. Winzler, Univ. of Ill. College of Med., 1853 W. Polk St., Chicago 11.

INDIANA†

Benedict E. Abreu, Pitman-Moore Co., 1200 Madison Ave., Indianapolis 6.
 Earl H. Antes, 412 S.E. 4th St., Evansville 9.
 Orville T. Bailey,** Larue D. Carter Memorial Hosp., 1315 W. Tenth St., Indianapolis 7.
 A. Ebner Blatt,** 3209 N. Meridian St., Indianapolis.
 James S. Browning,** 6146 N. Penn St., Indianapolis 20.
 Carl A. Bunde,** Pitman-Moore Co., 1200 Madison Ave., Indianapolis 6.
 Fred S. Carter, 402 E. Jefferson Ave., La Porte.
 J. Hal Doran, 720 Hume Mansur Bldg., Indianapolis.
 J. L. Elsaman, 427 W. Wiley, Bluffton.
 Robert B. Failey, Jr., 420 Hume Mansur Bldg., Indianapolis.
 Charles Fisch, 3120 N. Meridian, Indianapolis.
 Paul J. Fouts,** 522 Hume Mansur Bldg., Indianapolis.
 William D. Gambill,* 1911 N. Kessler Blvd., Indianapolis.
 Richard S. Griffith, Indianapolis General Hosp., Indianapolis.
 Laura Hare,** 23 E. Ohio St., Indianapolis.
 Oscar M. Helmer,** Indianapolis General Hosp., Indianapolis.
 Don Carlos Hines,** 740 S. Alabama St., Indianapolis 6.
 Charles E. Jackson, 303 S. Main St., Bluffton.
 William R. Kirtley, Lilly Research Labs., 740 S. Alabama St., Indianapolis 6.
 Kenneth G. Kohistaedt,** General Hosp., Lilly Lab., Indianapolis 7.
 I. J. Kwitny,** 3209 N. Meridian St., Indianapolis.
 Vincent L. Love, Davis Clinic, Marion.
 Robert J. Marvel, 3311 N. Meridian St., Indianapolis 8.
 Durward W. Paris,** 614 Armstrong-Landon Bldg., Kokomo.
 Franklin B. Peck,** Lilly Research Labs., Indianapolis 6.
 James D. Peirce, Lilly Labs. for Clinical Rsrch., Indianapolis.
 Arthur B. Richter,** 720 Hume-Mansur Bldg., Indianapolis 4.
 Wayne L. Ritter,** 312 Hume Mansur Bldg., Indianapolis 4.
 Carroll E. Roach,** Lilly Research Lab., Eli Lilly & Co., Indianapolis 6.
 Robert J. Rohn, 420 Hume Mansur Bldg., Indianapolis.
 Bernard D. Rosenak,** 23 E. Ohio St., Indianapolis.
 John S. Schechter,* 4966 Kingsley Dr., Indianapolis 5.
 Louis A. Schneider, 1351 W. Sherwood Terrace, Fort Wayne 6.

† See also Addenda, p. 143.

John A. Shively, 303 S. Main St., Bluffton.
 Wendell A. Shullenberger,** 3740 Central Ave., Indianapolis 5.
 Alfred T. Symmes,* 605 E. Maple Rd., Indianapolis 8.
 Morrie E. Thomas,** 445 N. Pennsylvania St., Indianapolis.
 Wallace S. Tirman,** 303 S. Main St., Bluffton.
 Clifford W. Ulrich,* 3433 Central, Indianapolis.
 Dan L. Urschel,** 108 E. Main, Mentone.
 Helen D. Van Vactor,* 226 Hume Mansur Bldg., Indianapolis.
 S. O. Waife, Med. Dept., Eli Lilly & Co., Indianapolis 6.
 C. G. Weigand,** 5234 N. Capitol Ave., Indianapolis 8.
 Kenneth R. Woolling, 5303 Boulevard Pl., Indianapolis 8.
 Woodson C. Young,* 428 Bankers Trust Bldg., Indianapolis.

IOWA

James T. Bradbury,** University Hosp., Iowa City.
 Elwood Buchman, 1325 Yewell St., Iowa City.
 Raymond G. Bunge,** University Hosp., Iowa City.
 James W. Culbertson, University Hosp., Iowa City.
 Richard D. Eckhardt, V. A. Hospital, Iowa City.
 Robert E. Hodges,* 118 Central Park, Iowa City.
 Walter M. Kirkendall, V. A. Hospital, Iowa City.
 Russell Meyers,** Univ. of Iowa Med. School, Iowa City.
 George Perret,** Univ. of Iowa Hosp., Iowa City.

KANSAS

Harold H. Jones, Jr.,* Snyder-Jones Clinic, Winfield.
 Franklin D. Murphy, Univ. of Kansas, Lawrence.
 George L. Norris,** 1401 E. 1st St., Winfield.
 E. J. Ryan, Emporia Gazette Bldg., Emporia.
 John S. Schweppe, 3217 Weston Rd., Topeka.
 H. Eugene Smith, Univ. of Kan., Med. Cntr., Kansas City 3.

KENTUCKY

Marion F. Beard,** 712 Francis Bldg., Louisville 2.
 John R. Gott, Jr.,** V. A. Hospital, Louisville 2.
 John S. Harter,** 1410 Castlewood Ave., Louisville 4.
 Joseph P. Holt,** Inst. for Med. Rsrch., Univ. of Louisville, 323 E. Chestnut St., Louisville 2.
 Carl W. Kumpe, 303 Doctors Bldg., Covington.
 Warren S. Rehm, Jr.,** 2067 Ravinia Ave., Louisville 5.
 Everett H. Sanneman, Jr., 712 Francis Bldg., Louisville 2.

Arthur M. Schoen, Univ. of Louisville, School of Med., 323 E. Chestnut St., Louisville 2.
 Alex J. Steigman, 101 W. Chestnut St., Louisville.
 Clayton B. Weed, Jr., 2128-1 U. S. Army Hosp., Fort Knox.
 Carroll L. Witten, 2233 Taylorsville Rd., Louisville 5.
 Irvin Zeavin, Cumberland Clinic, Cumberland.

LOUISIANA

George M. Anderson, 207 Weber Bldg., Lake Charles.
 Robert Birchall, Ochsner Clinic, Prytania & Aline Sts., New Orleans 15.
 Thomas C. Black,** V. A. Hospital, Alexandria.
 George E. Burch,** 1430 Tulane Ave., New Orleans 13.
 James A. Cronvich, 101 Colonial Club Dr., New Orleans 21.
 Harry E. Dascomb, 1542 Tulane Ave., New Orleans.
 William D. Davis, Jr., 7125 Benjamin St., New Orleans 18.
 Vincent J. Derbes, Tulane Univ., New Orleans.
 Douglas L. Gordon, Oschner Clinic, 3503 Prytania St., New Orleans.
 Marion W. Hood,** Charity Hosp. of La., New Orleans 13.
 Bernard M. Kalstone,* 6815 Southern Ave., Shreveport.
 Andrew Kerr, L.S.U. School of Med., 1542 Tulane Ave., New Orleans.
 Homer D. Kirgis, Ochsner Clinic, 3505 Prytania St., New Orleans 15.
 Nathaniel B. Kurnick, Tulane Univ. School of Med., 1430 Tulane Ave., New Orleans 12.
 Louis Levy, II, 1515 Aline, New Orleans 15.
 Carl S. Nadler, Jr., 3619 Prytania St., New Orleans 15.
 Philip Pizzolato,** Charity Hospital, New Orleans.
 Ralph V. Platou,** 1430 Tulane Ave., New Orleans.
 C. Thorpe Ray, Tulane Univ. Med. School, New Orleans 13.
 Wallace Sako,** Childrens' Clinic, Medical Arts Bldg., 3439 Prytania St., New Orleans 15.
 Otto Schales,** 3503 Prytania St., New Orleans 15.
 John H. Seabury,** La. State Univ. School of Med., New Orleans 13.
 Albert Segaloff, Alton Ochsner Med. Foundation, Prytania St., New Orleans 15.
 Charles C. Sprague,* Tulane Univ. Med. School, 1430 Tulane Ave., New Orleans 12.
 Ian Stevenson, School of Med., La. State Univ., New Orleans.
 Sam A. Threefoot, 3500 Prytania St., New Orleans 15.

Walter J. Trautman, Jr., 1441 Delachaise St., New Orleans.
 Walter G. Unglaub, Tulane Univ. School of Med., 1430 Tulane Ave., New Orleans.
 Neill K. Weaver, Tulane Univ. School of Med., 1430 Tulane Ave., New Orleans 12.
 C. Ray Womack, La. State Univ. School of Med., New Orleans 12.

MAINE

Robert L. Ohler, V. A. Hospital, Togus.

MARYLAND

James H. Baxter, National Inst. of Health, Bethesda 14.
 Richard J. Bing,** Johns Hopkins Hosp., Baltimore.
 Andrew J. Brennan,** 7725 Aberdeen Rd., Bethesda.
 Frederic G. Burke, 501 E. Woodbine, Chevy Chase.
 William V. Consolazio,** 23 Argyle Ave., Garrett Park.
 Ernest Cotlove, 10310 Dromm Ave., Kensington.
 Eugene P. Cronkite, National Naval Med. Cntr., Bethesda.
 John J. Curry, 11301 Georgia Ave., Silver Spring.
 James O. Davis, National Heart Institute, Bethesda.
 Leroy E. Duncan, Jr., 214 Chancery Rd., Baltimore 18.
 Leon Eisenberg, 1801 W. Baltimore St., Baltimore 23.
 Richard H. Ettinger,* 714 Northampton Dr., Silver Spring.
 Laurence Finberg, 4940 Eastern Ave., Baltimore 24.
 Sam T. Gibson, 5803 Anniston Rd., Bethesda 14.
 Aram Glorig,** 200 E. Indian Spring Dr., Silver Spring.
 Robert P. Grant, National Heart Institute, Bethesda.
 Monte A. Greer, 5908 Johnson Ave., Bethesda 14.
 William J. Harrington, National Inst. of Health, Bethesda 14.
 William M. Hart,** Natl. Inst. of Neurol. Diseases & Blindness, Bethesda 14.
 Roy Hertz,** National Cancer Institute, Bethesda.
 David S. Howell, National Heart Institute, Bethesda.
 Robert E. Hyatt, National Heart Institute, Bethesda 14.
 Thomas J. Kennedy, Jr., Pub. Health Serv., Natl. Inst. of Health, Bethesda 14.
 Milton Landowne, Baltimore City Hospital, Baltimore 24.
 Joseph L. Lihenthal, Jr.,** Johns Hopkins Hosp., Baltimore 5.
 James V. Maloney, Jr., Johns Hopkins Hosp., Baltimore.
 John H. Miller, 8806 Wolverton Rd., Baltimore 34.
 Stanley Miller, 914 N. Charles St., Baltimore 1.

George S. Mirick,** Johns Hopkins Univ. Med. School, Baltimore.
 William M. Mogabgab, Medical Dept., U.S.N.T.C., Bainbridge.
 Roger K. McDonald, 1608 Sherwood Ave., Baltimore 12.
 Marion E. McDowell, 716 Northampton Dr., Silver Spring.
 Jack Orloff, National Heart Institute, Bethesda.
 Gerald B. Phillips, National Institutes of Health, Bethesda 14.
 Harry Prystowsky, Johns Hopkins Hosp., Baltimore 5.
 Morton F. Reiser, 8414 10th Ave., Silver Spring.
 C. Martin Rhode, 1066 Second St., Perry Point.
 Marvin Rosecan, National Inst. of Health, Bethesda 14.
 Sidney Scherlis, 1214 N. Calvert St., Baltimore.
 Jacques L. Sherman, Jr., 2311 Churchill Rd., Silver Spring.
 N. Raphael Shulman, National Naval Med. Cntr., Bethesda 14.
 Van M. Sim,* Naval Unit, Army Chemical Center.
 Samuel S. Spicer, National Inst. of Health, 6 North Dr., Bethesda 14.
 Samuel J. N. Sugar,** 4300 Kaywood Dr., Mt. Rainier.
 Celia W. Tabor, 4 North Dr., Bethesda.
 Irene G. Tamagna, 4709 Montgomery Lane, Bethesda.
 Paul Teschan, 443 Southampton Dr., Silver Spring.
 Mackenzie Walser,* National Naval Med. Cntr., Bethesda 14.
 Donald M. Watkin, National Heart Institute, Baltimore 24.
 Janet Wolter,* Johns Hopkins Hosp., Baltimore 5.

MASSACHUSETTS†

Walter H. Abelman, Boston City Hosp., Boston 18.
 Mark Aisner,** 314 Commonwealth Ave., Boston.
 Fred H. Allen, Jr., 300 Longwood Ave., Boston 15.
 Leon T. Atlas, Peter Bent Brigham Hosp., 721 Huntington Ave., Boston 15.
 Charles C. Bailey, 1180 Beacon St., Brookline 46.
 Donald V. Baker, Jr., V. A. Hospital, Boston 18.
 Henry J. Bakst,** 80 E. Concord St., Boston 18.
 Francis G. Barnum,* 1776 Beacon St., Brookline.
 Theodore B. Bayles,** Robert Breck Brigham Hosp., 125 Parker Hill Ave., Boston.
 George O. Bell,** 82 Arnold Rd., Wellesley Hills 82.
 Patricia H. Benedict,** 264 Beacon St., Boston 16.
 Frederick S. Bigelow, 40 Vose's Lane, Milton.

Richard A. Bloomfield, 144 Commonwealth Ave., Boston 16.
 James F. Blute, Jr., 465 Walnut St., Fall River.
 Robert F. Bradley,* 100 Gerry Rd., Chestnut Hill 67.
 Elliott Bresnick, 68 Bay State Rd., Boston 15.
 Morton G. Brown,** 27 Alexander Rd., Newton Highlands.
 Belton A. Burrows, Evans Memorial Hosp., 65 E. Newton St., Boston 18.
 John J. Byrne, 818 Harrison Ave., Boston 18.
 John M. Cahill,* 35 Crowninshield Rd., Brookline.
 William B. Castle,** Thorndike Memorial Lab., Boston City Hosp., Boston 18.
 Thomas C. Chalmers, 1 Craigie St., Cambridge.
 Kenneth Chesky,* 468 Commonwealth Ave., Boston.
 Robert B. Chodos, V. A. Hospital, 150 S. Huntington Ave., Boston 30.
 William S. Clark, 46 Gleason Rd., Lexington 73.
 John F. Conlin,** 2 York Rd., Winchester.
 Peter H. Contompasis,* 4459 Washington St., Roslindale 31.
 John C. Corrigan,** 465 Walnut St., Fall River.
 John F. Crigler, Jr., Dept. of Biology, M.I.T., Cambridge 39.
 Perry J. Culver, Mass. General Hosp., Boston 14.
 T. D. Cuttle,** Naval Hospital, Chelsea 50.
 Donat Paul Cyr,** 605 Commonwealth Ave., Boston.
 Charles S. Davidson,** Boston City Hosp., Boston 18.
 Albert I. C. DeFriez, Hancock Village, Chestnut Hill 67.
 Jane F. Desforges, Boston City Hosp., Boston.
 Lewis Dexter,** 721 Huntington Ave., Boston.
 Alfred M. Donovan,* 45 Albion St., Wakefield.
 James Dow,* 458 Beacon St., Boston 15.
 Francis W. Drinan,* 45 Shornecliffe Rd., Newton.
 Franklin G. Ebaugh, Jr., Mass. Memorial Hosp., 750 Harrison Ave., Boston 18.
 William S. Elias, Lahey Clinic, Boston.
 Charles P. Emerson, Jr.,** Evans Memorial, 65 E. Newton St., Boston.
 Kendall Emerson, Jr.,** Peter Bent Brigham Hosp., Boston 15.
 Robert J. Fahey, 23 Bay State Rd., Boston.
 Bruce C. Ferguson, 40 St. John St., Jamaica Plain.
 Stuart C. Finch, 59 St. Paul St., Brookline.
 John J. Finn, Jr., 270 Commonwealth Ave., Boston 16.

† See also Addenda, p. 143.

- William H. Fishman, Tufts College Med. School, Boston.
 Joseph M. Foley, Neurological Unit, 818 Harrison Ave., Boston 18.
 Anne P. Forbes,** 304 Adams St., Milton.
 Peter H. Forsham, 366A Washington St., Canton.
 A. Stone Freedberg,** 330 Brookline Ave., Boston.
 Norbert Freinkel, Thorndike Memorial Lab., City Hospital, Boston.
 George J. Gabuzda, Jr., Thorndike Memorial Lab., City Hospital, Boston 18.
 Edward A. Gaensler, 249 River St., Mattapan 26.
 Frank H. Gardner, Peter Bent Brigham Hosp., Boston.
 Benjamin F. Gill,* V. A. Hospital, Boston 30.
 David Gitlin, Children's Hospital, Boston 15.
 Thomas M. Gocke, Thorndike Memorial Lab., City Hospital, Boston 18.
 Walter T. Goodale,** Peter Bent Brigham Hosp., Boston 15.
 Richard Gorlin, Peter Bent Brigham Hosp., 721 Huntington Ave., Boston.
 Garth K. Graham, 4 Casco Road, Lynn.
 Seymour J. Gray,** 721 Huntington Ave., Boston.
 William E. R. Greer, 235 Park Drive, Boston.
 Meyer H. Halperin, Evans Memorial Hosp., 65 E. Newton, Boston.
 Milton W. Hamolsky, Beth Israel Hosp., 330 Brookline Ave., Boston.
 Irwin B. Hanenson, 132 Beaconsfield Rd., Brookline 46.
 Philip H. Henneman, 18 Cushing Rd., Brookline 46.
 J. Aaron Herschfus, 5 Post Office Square, Sharon.
 Thomas F. Higgins,* Boston City Hosp., Boston.
 Freddy Homberger, Tufts College Med. School, 30 Bennet St., Boston 11.
 Justin M. Hope, 88 A. Chestnut St., Boston 8.
 Calderon Howe, Peter Bent Brigham Hosp., 721 Huntington Ave., Boston 15.
 Herbert Hyman,* Murphy Army Hosp., Waltham 54.
 Sidney H. Ingbar, 46 Kingswood Rd., Auburndale.
 Charles A. Janeway,** Children's Hospital, 300 Longwood Ave., Boston.
 Stewart H. Jones,** 210 Babcock St., Brookline 46.
 Walter E. Judson, Evans Memorial Hosp., 65 E. Newton St., Boston.
 Edward H. Kass, Thorndike Memorial Lab., City Hospital, Boston.
 Kermit Katz, 270 Commonwealth Ave., Boston.
 Rita M. Kelley,* 264 Beacon St., Boston 16.
 Robert W. Kistner,* Free Hospital for Women, Brookline.
 William S. Kiyasu, Children's Med. Cntr., 300 Longwood Ave., Boston 15.
 Henry J. Kowalski, Thorndike Memorial Lab., City Hospital, Boston.
 Philip Kramer, Evans Memorial Hosp., 65 E. Newton St., Boston 18.
 George S. Kurland, 330 Brookline Ave., Boston.
 Rodney C. Larcom, Jr., 390 High St., Westwood.
 Samuel E. Leard, Evans Memorial Hosp., 65 E. Newton St., Boston 18.
 Henry M. Lemon, 80 E. Concord St., Boston 18.
 Harold D. Levine,** 171 Bay State Rd., Boston 15.
 Leon Levinson, 483 Beacon St., Boston 15.
 Benjamin M. Lewis, Peter Bent Brigham Hosp., 721 Huntington Ave., Boston.
 Julius Litter, Evans Memorial Hosp., 65 E. Newton St., Boston 18.
 Joseph R. Lynch,** 1180 Beacon St., Brookline.
 William A. Lynch,* 1101 Beacon St., Brookline.
 James A. McA'Nulty,* 77 Bailey St., Dorchester 24.
 Janet W. McArthur, Mass. General Hosp., Boston 14.
 E. Lawson McDonald, Peter Bent Brigham Hosp., 721 Huntington Ave., Boston 15.
 Dougald C. MacGillivray,* 33 Hobson St., Brighton.
 John A. McGowan, N. E. Center Hosp., Bennet St. & Harrison Ave., Boston.
 John F. McManus,** 39 Bay State Rd., Boston.
 Thomas J. McNamara,* 18 Holbrook Ave., Lowell.
 Farahe Maloof, Mass. General Hosp., Fruit St., Boston.
 Benedict F. Massell,** 25 Binney St., Boston.
 J. K. Merlis, V. A. Hospital, 150 S. Huntington Ave., Boston 30.
 John P. Merrill, 564 Quinobequin Rd., Waban.
 James Metcalfe, 43 Wilshire Park, Needham.
 Jack Metcalf, 78 Chestnut Hill Rd., Brookline.
 Joseph M. Miller, 416 Marlboro St., Boston.
 Herbert P. Minkel,* 564 La Grange St., West Roxbury 32.
 William C. Moloney,** 39 Bay State Rd., Boston 15.
 George E. Morris,** 520 Commonwealth Ave., Boston.
 Albert S. Murphy,* 520 Commonwealth Ave., Boston.
 John C. Nemiah,* 42 Hawthorn St., Cambridge 38.
 George Nichols, Jr.,* Children's Hosp., 300 Longwood Ave., Boston.
 Nancy Nichols,* Baker Clinic Rsrch. Lab., N. E. Deaconess Hosp., Boston.
 John W. Norcross,** 29 Nod Hill Rd., Newton Highlands.
 Joseph J. O'Connor,* 172 Church St., West Roxbury 32.
 Arthur F. O'Keefe, 330 Dartmouth St., Boston 16.
 A. Seymour Parker, Jr.,* 605 Commonwealth Ave., Boston.
 Edwin W. Peterson,* 250 Stoughton St., Stoughton.
 Murray Rabinowitz,* Peter Bent Brigham Hosp., 721 Huntington Ave., Boston.
 Elliot Rapaport, 85 Undine Rd., Brighton 35.
 Robert W. Reifenshtein,* 335A Howard St., Cambridge.
 Arnold S. Relman, Evans Memorial Hosp., 65 E. Newton St., Boston 18.
 Stanley L. Robbins, Malloy Inst. of Path., City Hospital, Boston.
 Joseph Rogers, Joseph H. Pratt Diagnostic Hosp., Boston.
 Jack D. Rosenbaum, V. A. Hospital, S. Huntington Ave., Boston.
 Joseph F. Ross,** 65 E. Newton St., Boston.
 David I. Rutledge,** 605 Commonwealth Ave., Boston.
 David D. Rutstein,** Harvard Medical School, Boston.
 John T. Quinby, 264 Beacon St., Boston 16.
 Paul M. G. St. Aubin,* Mass. General Hosp., Boston 14.
 Robert Schwartz, Thorndike Memorial Lab., City Hospital, Boston 18.
 William B. Schwartz, New England Center Hosp., Boston.
 Jesse F. Scott, 72 W. Cedar St., Boston.
 Maurice S. Segal,** 370 Commonwealth Ave., Boston 15.
 Bertram Selverstone, New England Center Hosp., 171 Harrison Ave., Boston 11.
 Louis A. Selverstone, New England Center Hosp., Boston.
 Herbert S. Sise, 203 Commonwealth Ave., Boston.
 John H. Sisson, Evans Memorial Hosp., 65 E. Newton St., Boston 18.
 R. W. Sjogren,* 40 Fairfield St., Cambridge 40.
 Lloyd H. Smith, Jr., A-24 Winthrop House, Harvard Univ., Cambridge.

Carlton R. Soudors,** Lahey Clinic, 605 Commonwealth Ave., Boston.
 Malcolm Stanley, 136 Rawson Rd., Brookline 46.
 Joseph R. Stanton, 482 Beacon St., Boston 15.
 Richard H. Stanton, 482 Beacon St., Boston.
 Mario Stefanini, New England Center Hosp., 30 Bennet St., Boston.
 Lawrence Stellar, 314 Commonwealth Ave., Boston 15.
 Daniel Stowens, Children's Cancer Rsrch. Found., 35 Binney St., Boston 15.
 Maurice B. Strauss,** 27 Grove Hill Ave., Newtonville.
 Charles L. Sullivan,** 1101 Beacon St., Brookline.
 Hugh Tatlock, 264 Elm St., Northampton.
 Melvin L. Taymor, Evans Memorial Hosp., 65 E. Newton St., Boston.
 Louis Tobian, Jr., Dept. of Biochem., Harvard Med. School, Boston 15.
 Willard P. VanderLoan, Jr.,* 30 Bennet St., N. E. Center Hosp., Boston.
 Lawrence Van Selden,* 175 State St., Springfield.
 Hans Waine,** 51 Hampshire St., West Newton.
 William P. Walsh, 333 Union St., New Bedford.
 Paul F. Ware, 16 Norwich St., Worcester.
 Richard Warren,** 1180 Beacon St., Brookline 46.
 Thomas A. Warthin,** V. A. Hospital, Jamaica Plain 31.
 Elton Watkins, Jr., Children's Hosp., 300 Longwood Ave., Boston 15.
 C. Wesley Watson, Boston City Hospital, Boston.
 John M. Weller, 721 Huntington Ave., Boston 15.
 Thomas H. Weller, Children's Hosp., 300 Longwood Ave., Boston.
 Stanford Wessler, 330 Brookline Ave., Boston 15.
 Edwin O. Wheeler, Mass. General Hosp., Boston.
 James L. Whittenberger, 55 Shattuck St., Boston 15.
 Robert W. Wilkins,** Evans Memorial Hosp., 65 E. Newton St., Boston 18.
 Charles R. Williamson,* 1269 Beacon St., Brookline.
 Gordon D. Winchell,* 256 Woburn St., Lexington.
 Norman Zamcheck, Thorndike Memorial Lab., City Hospital, Boston.
 Louis Zetzel,** 17 Bay State Rd., Boston.
 Paul Zoll,** 330 Brookline Ave., Boston 15.

MICHIGAN†

Thomas W. Adams,* Wayne County General Hosp., Eloise.
 John D. Adcock,** Dept. of Internal Med., Univ. Hosp., Ann Arbor.
 Charles H. Altshuler, Wayne County General Hosp., Eloise.
 Arnold R. Axelrod, Wayne Univ., College of Med., 1512 St. Antoine St., Detroit 26.
 Harry Balberor,* 1404 David Brodrick Tower, Detroit 26.
 Paul S. Barker,** Dept. of Internal Med., Univ. Hosp., Ann Arbor.
 Thomas M. Batchelor, 7600 John Rd., Detroit 2.
 Jere M. Bauer, Dept. of Internal Med., Univ. Hosp., Ann Arbor.
 William H. Beierwaltes, Dept. of Internal Med., Univ. Hosp., Ann Arbor.
 Robert E. L. Berry, Univ. Hosp., Ann Arbor.
 Frank H. Bethell,** 409 Lenawee Dr., Ann Arbor.
 Ronald C. Bishop, Dept. of Internal Med., Univ. Hosp., Ann Arbor.
 Marvin J. Blaess,** 2707 Book Bldg. Tower, Detroit 26.
 Alexander Blain, III, Alexander Blain Hosp., 2201 E. Jefferson Ave., Detroit 7.
 Robert J. Bolt, 1708 Geddes Ave., Ann Arbor.
 Abraham I. Braude, Univ. Hosp., Ann Arbor.
 J. Marion Bryant, Univ. Hosp., Ann Arbor.
 Earl L. Burbidge,** Upjohn Company, Kalamazoo 99.
 William J. Butler, Peoples State Bank, St. Joseph.
 Eldon L. Caffery, Wayne County General Hosp., Eloise.
 Augusto A. Camara,* 818 E. University, Ann Arbor.
 Darrell A. Campbell,** St. Joseph's Mercy Hosp., Ann Arbor.
 Kenneth N. Campbell, Alexander Blain Hosp., 2201 Jefferson Ave. E., Detroit 7.
 A. A. Cintron-Rivera, Box 2001, 633 Church St., Ann Arbor.
 Armin A. Darmstaetter, Jr., 917 Glenhurst Dr. N., Birmingham.
 William G. Dixon,* 20451 Annapolis, Dearborn.
 Ivan F. Duff, Univ. Hosp., Ann Arbor.
 I. Donald Fagin, 18254 Livernois, Detroit 21.
 Stefan S. Fajans, 1216 Hutchins, Ann Arbor.
 Ben Fisher, Wayne County General Hosp., Eloise.
 George S. Fisher,** 10 Witherell St., Detroit 26.
 Francis S. Gerbasl, Univ. Hosp., Ann Arbor.

Robert W. Gillespie,* Box 171, Eloise.
 Herbert L. Goodman, Wayne Univ. College of Med., 1512 St. Antoine, Detroit 26.
 Alexander Gotz, 326 N. Ingalls, Ann Arbor.
 Ferdinand E. Greifenstein, 1512 St. Antoine St., Detroit 26.
 Thomas D. Grekin,* 18699 Muirland, Detroit 21.
 Harold F. Hailman, 301 Henrietta St., Kalamazoo.
 John E. Harroun, 306 Mathews Bldg., Owosso.
 Harper K. Helles, Wayne Univ. College of Med., 1512 St. Antoine St., Detroit 26.
 Allison B. Henderson,** 5320 John Rd., Detroit 2.
 Marshall I. Hewitt,* 5261 Chalmers, Detroit 13.
 Glenn I. Hiller, 397 Elmhurst, Highland Park 3.
 Sibley W. Hoobler,** 2228 Belmont Ave., Ann Arbor.
 Lloyd Iseri, 15941 Ellis St., Detroit 28.
 Samuel D. Jacobson, Wayne County General Hosp., Eloise.
 Elmer R. Jennings, Alexander Blain Hosp., 2201 E. Jefferson Ave., Detroit 7.
 Henry D. Kaine, 825 S. 1st St., Ann Arbor.
 William J. Kenfield, 3350 Campbell, Dearborn.
 Joyce W. Kingsley, Jr.,* 1372 Whittier, Grosse Pointe 30.
 Howard A. Klein, 1838 David Whitney Bldg., Detroit 26.
 Conrad R. Lam,** Henry Ford Hosp., Detroit.
 Andrew G. Lasichak, 908 Kales Bldg., Detroit 26.
 Alfred Lui,* Wayne County General Hosp., Eloise.
 William O. Maddock, Receiving Hosp., 1326 St. Antoine, Detroit 26.
 Otto T. Mallory, Jr.,** Univ. of Michigan Hosp., Ann Arbor.
 R. Ralph Margulis, 7624 Byron, Detroit 2.
 Kenneth P. Mathews, Dept. of Internal Med., Univ. Hosp., Ann Arbor.
 Paul E. Mattman, 1422 Seyburn Ave., Detroit 14.
 Muriel C. Meyers, 818 Lincoln, Ann Arbor.
 Raymond W. Monto, Henry Ford Hosp., Detroit 2.
 Robert Mosher, 2500 W. Grand Blvd., Providence Hosp., Detroit.
 Merle M. Musselman, Wayne County General Hosp., Eloise.
 Gordon B. Myers,** Wayne Univ. College of Med., Detroit.
 James V. Neel, Heredity Clinic, Univ. of Mich., Ann Arbor.
 William J. O'Hare, Jr.,* 136 Biltmore Dr., Inkster.

† See also Addenda, p. 143.

Alvin Paulsen, Receiving Hosp., 1326 St. Antoine, Detroit 26.
 Thomas D. Pemrick, Wayne County General Hosp., Eloise.
 H. Marvin Pollard,** Dept. of Internal Med., Univ. Hosp., Ann Arbor.
 William D. Robinson,** Dept. of Med., Univ. Hosp., Ann Arbor.
 Alva D. Rush,* Chrysler Corporation, Detroit 31.
 David J. Sandweiss,** 9739 Dexter Blvd., Detroit 6.
 Nelson H. Schimmel, Box 294, 575th Med. Sq., Selfridge.
 Charles L. Schneider, Wayne Univ. College of Med., Detroit 26.
 Henry K. Schoch,* Univ. Hosp., Ann Arbor.
 Holbrooke S. Seltzer, 1075 Conway Ct., Willow Run.
 D. Emerick Szilagyi,** 2799 West Grand Blvd., Detroit 2.
 E. Gifford Upjohn,** Upjohn Company, Kalamazoo.
 Alexander M. Waldron,** 1130 Hill St., Ann Arbor.
 Joseph P. Webb, Upjohn Company, Kalamazoo 99.
 Robert M. Whitrock, 1136 Michigan St., Ann Arbor.
 William Q. Wolfson, B-308 Univ. Hosp., Ann Arbor.
 Arnold Wollum,* 423 Section St., Norway.

MINNESOTA

E. D. Bayrd, 1116 Tenth St., S.W., Rochester.
 Craig W. Borden, University Heart Hosp., Minneapolis 14.
 Howard B. Burchell,** Mayo Clinic, Rochester.
 James Cain, Mayo Clinic, Rochester.
 Carleton B. Chapman, 1967 E. River Rd., Minneapolis 14.
 Charles F. Code,** Mayo Foundation, Rochester.
 Ephraim B. Cohen, 1047 Medical Arts Bldg., Minneapolis.
 James R. Cook,* Mayo Foundation, Rochester.
 Talbert Cooper, Mayo Clinic, Rochester.
 William H. Dearing,** Mayo Clinic, Rochester.
 James F. Hammarsten, V. A. Hospital, Minneapolis.
 Wallace E. Herrell,** 102 Second Ave., S.W., Rochester.
 Edgar A. Hines, Jr.,** Mayo Clinic, Rochester.
 Frederick W. Hoffbauer,** Dept. of Med., Univ. of Minn. Hosps., Minneapolis 14.
 Wyman E. Jacobson, 3015 Sumter Ave., Minneapolis 16.
 F. Raymond Keating, Jr.,** Mayo Clinic, Rochester.
 Frank E. Martin,* V. A. Hospital, Minneapolis.

John B. Moyer, Duluth Clinic, Duluth.
 Howard M. Odel,** Mayo Clinic, Rochester.
 Thomas W. Parkin, 102 2nd Ave., S.W., Rochester.
 Camen R. Paynter, 1202 4th Ave., S.W., Rochester.
 Ben Sommers,** 1232 Lowry Med. Arts Bldg., St. Paul 2.
 R. L. Varco, 420 N. Miss. River Blvd., St. Paul 4.
 Lewis W. Wannamaker, Univ. of Minn. School of Med., Minneapolis.
 W. Lane Williams, Univ. of Minn. School of Med., Minneapolis 14.
 Russell H. Wilson, V. A. Hospital, Minneapolis.

MISSISSIPPI

Norman Burnstein, V. A. Hospital, Jackson.
 Arthur C. Guyton, Univ. of Miss., University.
 S. Richardson Hill, Jr., Box 44, 3380th Med. Grp., Keesler A.F.B.
 John T. Lane,** 2228 Wilkes Ave., Biloxi.
 W. K. Purks,** Vicksburg Clinic, Vicksburg.
 Harold A. Sparr,** Olive Branch.

MISSOURI†

William H. Ames, 902 Edmond St., St. Joseph.
 Robert P. Bays, U. S. Med. Center, Springfield.
 Grace E. Bergner, 114 N. Taylor Ave., St. Louis 8.
 John W. Berry, 7261 Lindell, University City.
 Elwyn S. Brown,* 1512 Swallow Dr., Brentwood 17.
 Amos I. Chernoff, Washington Univ. Med. School, 600 S. Kingshighway, St. Louis 10.
 William H. Daughaday, 8333 Delmar Blvd., University City.
 Nannie K. M. de Leeuw, Barnes Hospital, 600 S. Kingshighway, St. Louis.
 Ben Eiseman, 600 S. Kingshighway, St. Louis.
 Gladden V. Elliott, 510 S. Kingshighway, St. Louis 10.
 Sarah M. Elliott,* City Hospital, 1515 Lafayette Ave., St. Louis.
 John T. Farrar, 8 Edgewood Rd., Ladue, St. Louis 5.
 Thomas B. Ferguson, 8528 Colonial Lane, Ladue 24.
 Robert J. Glaser, Barnes Hosp., St. Louis 10.
 David Goldring, 500 S. Kingshighway, St. Louis 10.
 David T. Graham, Barnes Hosp., 600 S. Kingshighway, St. Louis 10.
 Samuel B. Guze, Barnes Hosp., St. Louis 10.
 Arthur L. Haskins, 630 S. Kingshighway, St. Louis 10.

† See also Addenda, p. 143.

William G. Klingberg, St. Louis Children's Hosp., 500 S. Kingshighway, St. Louis 10.
 William A. Knight, Jr., 4161 Lindell Blvd., St. Louis 8.
 Virgil Loeb, Jr., 600 S. Kingshighway, St. Louis 10.
 Edward Massie,** 457 N. Kingshighway, St. Louis 8.
 Albert I. Mendeloff, 409 Oakley Dr., Clayton 5.
 J. Gerard Mudd, 1325 S. Grand, St. Louis 4.
 C. Barber Mueller, 600 S. Kingshighway, St. Louis.
 Adrian M. Ostfeld, 310 Belt Ave., St. Louis 12.
 Robert Paine, 5142 Waterman, St. Louis.
 Harry J. Price, V. A. Hospital, Poplar Bluff.
 Eli Robins, 4580 Scott, St. Louis.
 William B. Seaman, 510 S. Kingshighway, St. Louis 10.
 William A. Sodeman,** School of Med., Univ. of Mo., Columbia.
 John C. Tinsley, Jr.,* Ellis Fischel State Cancer Hosp., Columbia.
 Edward B. Williams, Jr., Homer G. Phillips Hosp., St. Louis.
 Keith S. Wilson,** 4952 Maryland Ave., St. Louis.

MONTANA

A. K. Atkinson, Box 911, Great Falls.
 John S. Gilson,* 109 23rd St., N., Great Falls.
 Earl L. Hall, Great Falls Clinic, Great Falls.
 Eugene Hildebrand, Mont. Deaconess Hosp., Great Falls.
 Laurence L. Howard,** 410 Central Ave., Great Falls.
 John A. Layne,** Great Falls Clinic, Great Falls.
 Frank L. McPhail,** Great Falls Clinic, Great Falls.
 Ferdinand R. Schemm,** Great Falls Clinic, Great Falls.

NEBRASKA

F. Lowell Dunn,** Medical Arts Bldg., Omaha 2.
 Paul Heller, V.A. Hospital, Omaha 5.
 Richard B. Johnson, 4911 Davenport St., Omaha.
 Kenneth F. Kimball,* 6220 Maple St., Omaha 4.
 Roy J. Korn, V.A. Hospital, 4101 Woolworth Ave., Omaha.
 Henry J. Lehnhoff, Jr.,** 607 Med. Arts Bldg., Omaha 2.
 Peyton T. Pratt, Univ. Hosp., 42nd & Dewey Ave., Omaha.
 Richard N. Reedy, 4114 N. 48th St., Omaha 4.
 Alvin Somberg,* Univ. of Nebr. Hosp., Omaha.
 John R. Walsh, 2105 Evans St., Omaha.
 Charles M. Wilhelmj,** Creighton Univ., Omaha 2.

Richard Young,** 1436 Medical Arts Bldg., Omaha.
Hyman J. Zimmerman, V.A. Hospital, 4101 Woolworth Ave., Omaha 5.

NEW HAMPSHIRE

William M. Chambers, Hitchcock Clinic, Hanover.
James T. Heyl, Phillips Exeter Acad., Exeter.
F. Corbin Moister, Hitchcock Clinic, Hanover.
Jan Nyboer,** Dartmouth Med. School, Hanover.
Richmond W. Smith, Jr., 26 Elliot St., Exeter.

NEW JERSEY

Robert W. Barnett,* 601 Grand Ave., Asbury Park.
Wilbur M. Benson, 133 Young Ave., Cedar Grove.
Paul K. Boyer,** 129 Summit Ave., Summit.
M. J. Brennan, 1301 ASU USA Hosp., Fort Monmouth.
Miles E. Drake, Vineland State School, Vineland.
David J. Lehman, Jr.,* 192 Roseville Ave., Newark 7.
Maxwell L. Littman, 16 Valley Pl., Tenafly.
Joan H. Long, 119 Lafayette Ave., Haddonfield.
Marvin Moser, 28 N. Crescent, Maplewood.
Edward R. Neary,** 210 Carlton Terrace, Teaneck.
Jay A. Robinson, 1757 S. Broad St., Trenton 10.
Jacob Rosenkrantz, V.A. Hosp., East Orange.
Leo H. Siegel,* 234 Roseville Ave., Newark 7.
J. James Smith, 626 Westminster Ave., Elizabeth.
William J. Snape, 573 Stevens St., Camden.
Henry A. Strade, 404 Ridgewood Ave., Glen Ridge.

NEW MEXICO

Paul H. Noth,** Los Alamos Hosp., Los Alamos.

NEW YORK

David Adlersberg,** Mount Sinai Hosp., New York 29.
Ellery G. Allen,** 508 State Tower Bldg., Syracuse 2.
Thomas P. Almy, 525 E. 68th St., New York 21.
Reginald M. Archibald,** Rockefeller Inst. Hosp., 66th St. & York Ave., New York 21.
Charles A. Ashley, % Waite, 3 Tanglewyde Ave., Bronxville.
J. Howland Auchincloss, Jr.,* Med. Dept. Univ. Hosp., 150 Marshall St., Syracuse 10.
Robert Austrian, F Bldg., Kings County Hosp., Brooklyn 3.

Harold G. Barker, Columbia Presbyterian Med. Cntr., 622 W. 168th St., New York 32.

Wayne Barker, 40 E. 83rd St., New York.

O. J. Bateman, 40 North St., Buffalo.

Stanley Batkin,* Univ. Hosp. of Good Shepherd, 150 Marshall St., Syracuse 10.

Ernest L. Becker,* N.Y.U. Bellevue Med. Cntr., 477 First Ave., New York 16.

Harold Bedell, 105 E. 73rd St., New York 21.

Morris B. Bender,** 1150 Park Avenue, New York.

Joseph G. Benton, N.Y.U. Bellevue Med. Cntr., 400 E. 34th St., New York 16.

Adolph R. Berger,** 22 E. 36th St., New York 16.

Eugene Y. Berger, Goldwater Memorial Hosp., Welfare Island New York 17.

Philip S. Bergman, 60 E. 67th St., New York 21.

William H. Bergstrom, Syracuse Memorial Hosp., Syracuse 10.

Leon G. Berman,** 713 E. Genesee St., Syracuse.

Stanley H. Bernstein,* USAF Hospital, Sampson.

Lester J. Besen,* 86 Spruce St., Yonkers.

Harry F. Bisel,* Memorial Hosp., 444 E. 68th St., New York 21.

Grovesnor W. Bissell, V.A. Hospital, 3495 Bailey Ave., Buffalo 15.

Marvin L. Bloom,* 333 Linwood Ave., Buffalo 9.

J. Leonard Brandt, 230 Park Pl., Brooklyn 17.

Robert Broh-Kahn,** Lasdon Foundation, Yonkers 2.

Henry Brown, 133 E. 58th St., New York 22.

Herbert R. Brown, Jr.,** Strong Memorial Hosp., Rochester.

Roswell K. Brown,** 596 Delaware Ave., Buffalo.

Maurice Bruger,** 45 Gramercy Park, N., New York 10.

Morton S. Bryer, 271 Central Park W., New York 24.

Kenneth W. Buchwald,** 663 N. Oak St., Buffalo 3.

Paul A. Bunn, Dept. of Med., Univ. Hosp., Syracuse 10.

Ivan Lee Bunnell, Univ. of Buffalo Med. School, Buffalo.

Daniel Burdick,* 211 Medical Arts Bldg., Syracuse 2.

Robert B. Burton, 260 Crittenden Blvd., Rochester 7.

J. Scott Butterworth,** 121 E. 60th St., New York.

Anthony Caccese, 7224 14th Ave., Brooklyn 28.

Francis S. Caliva, 508 Prospect Ave., Syracuse 8.

Henry A. Carr,** 232 E. 66th St., New York 21.

Anne C. Carter, 525 E. 68th St., New York 21.

Asher S. Chapman,** Oyster Bay Diagnostic Center, Oyster Bay.

William H. C. Chapple, 2577 Main St., Buffalo.

Maurice R. Chassin, 61-42 Maspeth Ave., Maspeth.

Abraham G. Cohen,** 52 E. 73rd St., New York 21.

Eugene J. Cohen, 525 E. 68th St., New York 21.

Henry Colcher, 408 W. 255th St., New York 71.

William S. Collens,** 123 8th Ave., Brooklyn.

Harvey S. Collins, Memorial Hosp., 444 E. 68th St., New York 21.

Vincent J. Collins, St. Vincents Hosp., 145 W. 11th St., New York 11.

A. Dale Console, 745 Fifth Ave., New York 22.

Albert W. Cook, 622 A Third St., Brooklyn 15.

Irving S. Cooper, 477 First Ave., New York 16.

Charles B. Crow,* Rodriguez Army Hosp., APO 851, PM, New York.

Simon Dack,** 122 E. 78th St., New York.

Michael M. Dacso, Goldwater Memorial Hosp., Welfare Island, New York 17.

Arthur C. De Graff,** 850 Park Ave., New York 21.

Clarence Dennis,** Kings County Hosp., 451 Clarkson Ave., Brooklyn.

Henry Diamond, Memorial Hosp., East 68th St., New York.

Robert Dicks, 1304 Ditmar Ave., Brooklyn 26.

H. Leo Dickson,** Bristol Laboratories, Inc., Syracuse.

James A. Dingwall, 11 East 68th St., New York 21.

William R. Dorrance, 35-C Picotte Dr., Albany.

Henry Doubilet,** 71 East 77th St., New York 21.

James Ducey, Roosevelt Hosp., New York.

Benedict J. Duffy, Univ. of Rochester School of Med., Rochester.

John J. Duggan, State Univ. of N. Y. Med. Coll., Syracuse 10.

Samuel Dvoskin, 200 Cabrini Blvd., New York 33.

David P. Earle, Jr.,** Goldwater Memorial Hosp., New York.

John N. Edson, 142 Joralemon St., Brooklyn.

Clifford J. Edwards, 36 Campbell Ave., Williston Park.

Rose R. Ellison, 70 Haven Ave., New York 32.

Samuel K. Elster, Mount Sinai Hosp., New York.

Herbert K. Ensworth,** 608 E. State St., Ithaca.

Frederick H. Epstein, 190-20 37th Ave., Flushing, L.I.
 John F. Fairbairn, II,* 100 High St., Buffalo 3.
 William W. Faloona, Univ. Hosp. of Good Shepherd, Syracuse 10.
 Saul J. Farber, 1 74th St., Brooklyn 9.
 Aaron Feder, 40-42 75th St., Jackson Heights 73.
 Daniel J. Feldman, 850 Park Ave., New York 21.
 Harry A. Feldman, Dept. of Med., Univ. Hosp., Syracuse.
 M. Irene Ferrer, 10 E. 66th St., New York 21.
 Joseph W. Ferrebee,** Fable Farm, Cooperstown.
 Leonard E. Field,** 125 E. 72nd St., New York 21.
 Giles F. Filley, 166 Park Ave., Saranac Lake.
 John A. Finkbeiner, Memorial Center, 444 E. 68th St., New York 21.
 Edward E. Fischel, Presbyterian Hosp., 622 W. 168th St., New York.
 Martin M. Fisher,** 135 Fenimore St., Brooklyn 25.
 Gerald H. Flamm, 142 Joralemon St., Brooklyn 1.
 James Flexner,** Cricklewood Lane, Harrison.
 William T. Foley,** 2 E. 54th St., New York 22.
 Noble O. Fowler, Brooklyn Hospital, Brooklyn.
 Charles L. Fox, Jr.,** N. Y. Med. Coll., 1 E. 105th St., New York 29.
 Charles W. Frank,* 66 Wood Ave., Ardsley.
 Thomas F. Frawley, Albany Hospital, Albany.
 Charles K. Friedberg,** 1088 Park Ave., New York.
 Herman F. Froeb, 114-15 Union Turnpike, Forest Hills.
 Joseph W. Gardella,* 25 Main St., Cooperstown.
 Lytt I. Gardner, State Univ. of N. Y., Dept. of Ped., School of Med., Syracuse.
 Herbert Gershberg, N. Y. Univ. Med. School, 477 First Ave., New York.
 Burton Giges, Hosp. of Rockefeller Inst., 66 & York Ave., New York 21.
 Victor Ginsberg, 255 Eastern Parkway, Brooklyn 16.
 George B. J. Glass,** 53 E. 96th St., New York 28.
 Arvin S. Glickman, Memorial Center, 444 E. 68th St., New York 21.
 Helen Goodell,** 525 E. 68th St., New York 21.
 Abraham Gootnick,** V.A. Hospital, Fort Hamilton, Brooklyn.
 Irving Gordon, Div. of Labs. & Rsrch., New Scotland Ave., Albany 1.

William J. Grace, 525 E. 68th St., New York 21.
 Irving Graef,** 360 E. 55th St., New York 22.
 Louis W. Granirer,** 90-36 149th St., Jamaica.
 Milton Greenberg,* 1300 Cornaga Ave., Far Rockaway.
 David G. Greene, Buffalo General Hosp., 100 High St., Buffalo 3.
 Richard W. Greene, 238 Kensington Pl., Syracuse 10.
 Irving Greenfield,** 799 Central Ave., Woodmere, L. I.
 Ezra M. Greenspan, 1160 Fifth Ave., New York 29.
 Roger L. Greif, Hosp. of Rockefeller Inst., 66th St. & York Ave., New York 21.
 Arthur Grishman, 1176 Fifth Ave., New York 29.
 Albert W. Grokoest, 115 E. 67th St., New York 21.
 Edward B. Grossman,** Veterans Administration, 252 Seventh Ave., New York.
 Richard Gubner,** 25 Lefferts Ave., Brooklyn.
 Ramsdell Gurney,** 537 Delaware Ave., Buffalo.
 Jacob P. Halperin, 3306 Crescent St., Astoria 6.
 Jacob Halpern, 1012 Ave. K, Brooklyn.
 James H. Hammond,** Ramey Air Force Base, APO 845, PM, New York.
 Milton B. Handelsman,** 142 Joralemon St., Brooklyn 2.
 Albert H. Harris,** Loudonville.
 Jay Harris,* State Univ. of N. Y. Med. Cntr., Syracuse.
 Rejane M. Harvey, 10 E. 66th St., New York 21.
 James G. Hilton, 115 E. 67th St., New York 21.
 Lawrence E. Hinkle, New York Hosp., 525 E. 68th St., New York 21.
 William M. Hitzig,** 787 Park Ave., New York.
 Harold B. Houser, Wieting-Johnson Hosp., 960 Salt Springs Rd., Syracuse 3.
 Joe W. Howland,** 260 Crittenden Blvd., Rochester.
 Edward C. Hughes,** 713 E. Genesee St., Syracuse 2.
 L. Edgar Hummel,** 537 Delaware Ave., Buffalo.
 Allen E. Hussar,** V.A. Hospital, Montrose.
 Irving Innerfield, 58 N. Broadway, Nyack.
 Raymond S. Jackson, 34 Cathedral Ave., Hempstead.
 Ralph F. Jacox, 260 Crittenden Blvd., Rochester.
 Harry L. Jaffe,** 969 Park Ave., New York.
 Henry D. Janowitz, Mount Sinai Hosp., 1 E. 100th St., New York 29.
 Ralph A. Jessar, 622 W. 168th St., New York 32.

Mennasch Kalkstein,** 240 Central Park S., New York.
 Jerald S. Kalter, 18 E. 62nd St., New York 21.
 William M. Kelly,* 210 W. Sixth St., Elmira.
 Francis E. Kenny,** 109 Linwood Ave., Buffalo.
 David H. Klasson,** 129 Clarkson Ave., Brooklyn 26.
 Abbie I. Knowlton, 4963 Riverdale Ave., New York.
 Henry J. Koch, Jr., Memorial Center, 444 E. 68th St., New York 21.
 Howard P. Kreiger,* 167 Pebble Lane, Hewlett.
 Stuart Krohn,** 18 Hopper St., Utica 2.
 Irving G. Kroop, 20 Plaza St., Brooklyn 13.
 Herbert S. Kupperman, Coll. of Med., N. Y. Univ., 477 First Ave., New York 16.
 John S. La Due,** Pack Medical Group, 139 E. 36th St., New York 16.
 Eugene G. Laforet,* Hermann M. Biggs Hosp., Ithaca.
 Richard P. Lasser, 1159 E. 24th St., Brooklyn 10.
 Stanley L. Lee, 48 E. 91st St., New York 28.
 Samuel R. Lehrman, 100 W. 55th St., New York 19.
 Alfred R. Lenzner, 685 Delaware Ave., Buffalo 9.
 Stephen H. Leslie, N.Y.U. Coll. of Med., 477 First Ave., New York.
 Stanley Lesse,* 227 Central Park W., New York 24.
 Leon M. Levitt, 14 E. 16th St., Brooklyn.
 Marvin F. Levitt, Mt. Sinai Hosp., 5th Ave. & 100th St., New York 29.
 Tracy Levy, U.S.P.H.S. Hosp., Staten Island 4.
 Allyn B. Ley, 444 E. 68th St., New York 21.
 Robert M. Lintz,** 1100 Park Ave., New York 28.
 Charles W. Lloyd, Syracuse Med. College, Irving Ave., Syracuse.
 Maxwell L. Lockie,** 40 North St., Buffalo 2.
 Elmer H. Loughlin, 142 Joralemon St., Brooklyn 2.
 Winifred C. Loughlin,** 1100 Park Ave., New York 28.
 Edward W. Lowman, 400 E. 34th St., New York 16.
 Eugene Lozner, Univ. Hosp. of Good Shepherd, Syracuse 10.
 Hugh Luckey, 2nd Med. Div., Bellevue Hosp., Foot of E. 26th St., New York.
 A. Leonard Lubby, Flower-Fifth Ave. Hosps., New York.
 Daniel S. Lukas, New York Hosp., 525 E. 68th St., New York 21.
 Richard H. Lyons,** 150 Marshall St., Syracuse 10.

- Bernard Maisel, 525 E. 68th St., New York 21.
- Edgar P. Mannix, Jr., 7539 Kessel St., Forest Hills.
- Robert Margolis,* 546 LaFayette Ave., Brooklyn 5.
- Lester C. Mark, 1648 Vincent Court, Wantagh, L.I.
- Morton Marks, 400 E. 34th St., New York 16.
- Charles D. Marple,** American Heart Assn., 44 E. 23rd St., New York 10.
- Arthur M. Master,** 125 E. 72nd St., New York 21.
- Joseph P. Masterton,* 165 Niagara Falls Blvd., Buffalo 23.
- James A. L. Mathers,** 622 W. 168th St., New York 32.
- Raymond S. Megibow, 1050 Park Ave., New York 28.
- Robert C. Mellors, 47 Oakwood Ave., Rye.
- Milton Mendlowitz,** 136 E. 64th St., New York.
- John K. Meneely, Jr., Union Univ., Albany Med. Coll., Albany 3.
- Leo M. Meyer,** 550 E. 16th St., Brooklyn 26.
- Frank Meyers,** 537 Delaware, Buffalo.
- William J. Michaels, Jr., 831 James St., Syracuse 3.
- Max B. Milberg, 446 Ocean Ave., Brooklyn 26.
- George E. Miller, Buffalo General Hosp., 100 High St., Buffalo 3.
- Gerald Miller, Strong Memorial Hosp., 260 Crittenden Blvd., Rochester 20.
- John K. Miller,** Div. of Labs. & Rsrch., N. Y. State Dept. of Health, Albany 1.
- David W. Molander, 139 E. 36th St., New York 16.
- Herbert R. Morgan, Univ. of Rochester Med. School, Rochester.
- Carl Muschenheim,** 525 E. 68th St., New York 21.
- James E. McCormack,** Columbia University, Coll. of P. & S., 630 W. 168th St., New York 32.
- Walsh McDermott,** 525 E. 68th St., New York 21.
- Fletcher H. McDowell, 525 E. 68th St., New York 21.
- Teresa McGovern,** 123 E. 53rd St., New York 22.
- Morton Nathanson, N. Y. U., 477 First Ave., New York.
- C. Truman Nelson,** Presbyterian Hosp., 180 Ft. Washington Ave., New York 32.
- William P. Nelson, III,* 17 Crestwood Court, Albany.
- Erwin Neter,** Children's Hosp., 219 Bryant St., Buffalo 9.
- Charles Neuman, 2 Schuylen St., New Rochelle.
- William A. O'Brien, Jr., Strong Memorial Hosp., Rochester.
- Hugh B. O'Donnell,* 4501 Avenue H, Brooklyn.
- Elliot Oppenheim, 25 Central Park W., New York 23.
- Robert O. Oseasohn, Tropical Research Lab., APO 851, % PM, New York.
- James E. Patterson,** 312 Middlesex Road, Buffalo 2.
- John M. Pearce,** 525 E. 68th St., New York 21.
- Morris Pearlmutter, 54 E. 61st St., New York 21.
- Olof Pearson, 36 Garretson Rd., White Plains.
- Louis Felner,** 1352 Carroll St., Brooklyn.
- James E. Perkins,** 9 Hawthorne Rd., Bronxville.
- Mary L. Petermann,** 444 E. 68th St., New York 21.
- Anastas T. Petro, 444 E. 68th St., New York 21.
- Richard F. Platzer, Clifton Springs Sanitarium & Clinic, Clifton Springs.
- Albert A. Pientl, 14 Sutton Place S., New York.
- Charles M. Plotz, 1183 E. 23rd St., Brooklyn 10.
- Charles A. Poindexter,** 121 E. 60th St., New York.
- Leon Pordy, 1150 Park Ave., New York 28.
- Aurelia Potor,** 1078 Madison Ave., New York 28.
- John Prior, 766 Irving Ave., Syracuse 10.
- Arthur B. Raffi,** 713 E. Genesee St., Syracuse.
- Hyman Rappaport,** 37-27 103rd St., Corona, L.I.
- Robert W. Raymond,* 75 Willett St., Albany.
- Walter Redisch,** 10 E. 78th St., New York.
- Norbert B. Reicher, 712 E. Jefferson St., Syracuse 3.
- G. H. Reifenshtein,** 1801 State Tower Bldg., 109 S. Warren St., Syracuse.
- Edward H. Reisner, 401 W. 118th St., New York 27.
- Paul A. Riemenschneider, 210 Highland Ave., Syracuse.
- Harold Rifkin, 20 W. 86th St., New York.
- Seymour H. Rinzler, 120 Central Park S., New York 19.
- Norton D. Ritz, 2729 Bedford Ave., Brooklyn 10.
- Leonard W. Ritzmann,* 98 General Hosp., APO 108, PM, New York.
- Alvin L. Robins,* 54 Riverside Dr., New York 24.
- Walter F. Rogers, Jr., 102 Woodside Dr., Syracuse.
- Irving M. Rollins,* 875 Far Rockaway Blvd., Far Rockaway.
- Martin C. Rosenthal, Mount Sinai Hosp., 1 E. 100th St., New York 29.
- Hendrick M. Rozendaal,** 2128 Rosendale Rd., Schenectady.
- Bernard A. Sachs, 40 Leighton Ave., Yonkers 5.
- Udall J. Salmon,** 875 Fifth Ave., New York.
- Martin Sanders,* Mount Sinai Hosp., 100th St. & 5th Ave., New York.
- Ernest L. Sarason, 608 E. Genesee St., Syracuse.
- Arthur Sawlitsky, 15 The Hemlocks, Roslyn.
- Jerome A. Schack, 975 Park Ave., New York 28.
- Louis E. Schaefer, 144 Bard Ave., Staten Island 10.
- Peter P. Schmidt,* 269 N. Merrick Ave., Merrick.
- Ralph F. Schneider,** 72 Third Street, Garden City, L.I.
- John B. Schwedel,** 230 W. 79th St., New York 24.
- J. Edwin Seegmiller, Public Research Inst., Foot of E. 15th St., New York 9.
- David Selman,* 24 S. Main St., Spring Valley.
- Mortimer F. Shapiro, 815 Park Ave., New York 21.
- Martin A. Shearn, 147-45 75th Ave., Flushing.
- Joseph F. Shortleeve,* 11 Parkway, Larchmont.
- Bernard B. Siegel,* 1301 Cornaga Ave., Far Rockaway.
- Santos Silva, Pack Med. Group, 139 E. 36th St., New York.
- Harold M. Silver, 89-21 153rd St., Jamaica, L.I.
- Solomon Silver,** 14 E. 75th St., New York 21.
- Jonas H. Sirota, 325 Riverside Dr., New York.
- Howard B. Slavin,** 260 Crittenden Blvd., Rochester.
- Marvin H. Slesinger, 525 E. 68th St., New York 21.
- Robert J. Soberman, Bellevue Hosp., 28th St. & First Ave., New York.
- A. Alfred Solomon,** Diplomate Am. Bd. of Urology, 769 Empire Ave., Far Rockaway.
- Eugene Somkin,** 130 E. 94th St., New York.
- S. Zelig Sorkin,** 1148 Fifth Ave., New York.
- Chester M. Southam, Sloan-Kettering Inst., 444 E. 68th St., New York 21.
- Clifford L. Spingarm, 51 E. 73rd St., New York 21.
- Samuel H. Spitz,** 25 Monroe Pl., Brooklyn 2.
- Daniel Stats,** 129 E. 79th St., New York 21.
- Herman Steinberg, 525 E. 68th St., New York 21.
- Israel Steinberg,** 170 E. 77th St., New York 21.
- Morris F. Steinberg,** 50 E. 63rd St., New York 21.
- Alfred Steiner,** 53 E. 66th St., New York 21.
- Gene H. Stollerman, 555 Broadway, Hastings-on-Hudson.
- Scott N. Swisher, 260 Crittenden Blvd., Rochester 20.

Marguerite P. Sykes, 435 E. 52nd St., New York.
 Henry J. Tagnon,** Memorial Hosp., 444 E. 68th St., New York 21.
 Felix Taubman,* 115 Eastern Parkway, Brooklyn.
 Robert C. Taymor,* 820 Park Ave., New York.
 Ralph Tompsett, 525 E. 68th St., New York 21.
 Lester Tuckman,** 71 E. 77th St., New York 21.
 Robert Turell,** 25 E. 83rd St., New York 21.
 Louis B. Turner, Mt. Sinai Hosp., 5th Ave. & 100th St., New York 29.
 John H. Vaughan, Neurological Inst., Columbia Med. Cntr., New York.
 Stuart L. Vaughan,** 187 Linwood Ave., Buffalo 9.
 Louis J. Vorhaus, 3103 Fairfield Ave., Riverdale 63.
 Leo J. Wade,** Esso Standard Oil Co., 15 W. 51st St., New York 21.
 Bernard M. Wagner, Mt. Sinai Hosp., New York.
 Samuel Waldman,** 1401 President St., Brooklyn 13.
 John V. Waller,** 1 E. 69th St., New York 21.
 F. Charles Warren,** 200 Hicks St., Brooklyn.
 Louis R. Wasserman,** 4 E. 88th St., New York 28.
 Christine Waterhouse, Strong Memorial Hosp., 260 Crittenden Blvd., Rochester 20.
 William J. Waters, 705 State Tower Bldg., Syracuse.
 R. Janet Watson, 235 Adams St., Brooklyn 1.
 Aaron Weisberg, 1171 Eastern Parkway, Brooklyn 13.
 Lothar Wertheimer,* 179-25 Kildare Rd., Jamaica, L.I.
 Laurence G. Wesson, Jr., 477 First Ave., New York.
 Charles D. West, 86 Trenton Ave., White Plains.
 John Robert West, Coll. of Physicians & Surg., Columbia Univ., 620 W. 168th St., New York 32.
 W. W. Westerfield, State Univ. of N. Y., Med. Coll. at Syracuse, Syracuse.
 Robert E. Westlake, 713 E. Gene-see St., Syracuse 2.
 Raymond E. Weston, Montefiore Hosp., New York 67.
 Charles H. Wheeler, Jr.,** 260 E. 66th St., New York 21.
 Abraham C. White, Mt. Sinai Hosp., 1 E. 100th St., New York.
 Walter S. Wiggins, 328 Radcliffe Rd., RD 3, East Syracuse.
 Nathan D. Wilensky,** 1908 Ave. K, Brooklyn 30.
 Charles F. Wilkinson, Jr., N. Y. U. Med. School, 477 First Ave., New York.
 Harold Willard, New York Hosp., 525 E. 68th St., New York 21.

John R. Williams, Jr.,** 388 Monroe Ave., Rochester 7.
 Warren H. Williams,* Univ. Hosp., Marshall St., Syracuse.
 Arthur W. Wright,** Albany Med. Coll., Albany 3.
 Irving S. Wright,** 525 E. 68th St., New York 21.
 Felix Wroblewski, 1095 E. 10th St., Brooklyn 30.
 Tryee C. Wyatt,** Medical Arts Bldg., Syracuse.
 Lawrence E. Young, 260 Crittenden Blvd., Rochester 7.
 Walter T. Zimdahl, 2183 Main St., Buffalo 14.

NORTH CAROLINA†

Thomas B. Barnett, N. C. Memorial Hosp., Chapel Hill.
 Morton D. Bogdonoff, Dept. of Med., Duke Univ., Durham.
 Ivan W. Brown, Jr., Duke Univ. Hosp., Durham.
 Charles H. Burnett, U. of N. C. Med. School, Chapel Hill.
 David Cayer, Bowman Gray School of Med., Winston-Salem.
 Ernest Craigie, N. C. Memorial Hosp., Chapel Hill.
 Edward C. Curnen, Jr.,** U. of N. C. Med. School, Chapel Hill.
 Courtland H. Davis, Jr., Bowman Gray School of Med., Winston-Salem.
 Marcus L. Dillon, Box 2900, Duke Hosp., Durham.
 Janet J. Fischer, Dept. of Med. Univ. of N. C., Chapel Hill.
 Carl W. Gottschalk, N. C. Memorial Hosp., Chapel Hill.
 Harold D. Green,** Bowman Gray School of Med., Winston-Salem.
 Keith S. Grimson,** Duke Hosp., Durham.
 George C. Ham, U. of N. C. Med. School, Chapel Hill.
 George T. Harrell, Jr.,** Bowman Gray School of Med., Winston-Salem 7.
 John B. Hickam, Duke Hosp., Durham.
 Bernard C. Holland, Duke Hosp., Durham.
 Lucile W. Hutaff, Bowman Gray School of Med., Winston-Salem.
 Grace P. Kerby, Duke Hosp., Durham.
 E. Charles Kunkle, Duke Univ. School of Med., Durham.
 Jessica H. Lewis, U. of N. C. School of Med., Chapel Hill.
 Harold J. Magnuson, School of Pub. Health, U. of N. C., Chapel Hill.
 Samuel P. Martin, 113 Pinecrest Rd., Durham.
 Philip Morgenstern, V.A. Hospital, Swannanoa.
 Jack D. Myers, Duke Hosp., Durham.
 Jeffress G. Palmer, U. of N. C. School of Med., Chapel Hill.

† See also Addenda, p. 143.

John B. Pfeiffer, Jr., Box 3508, Duke Hosp., Durham.
 R. Wayne Rundles,** Duke Hosp., Durham.
 Robert E. Schell,* V.A. Hosp., Swannanoa.
 Theodore B. Schwartz, Dept. of Med., Duke Univ., Durham.
 Will Camp Sealy, Duke Hosp., Durham.
 John T. Sessions, Jr., U. of N. C. School of Med., Chapel Hill.
 Eugene A. Stead, Jr.,** Duke Univ. School of Med., Durham.
 Hack U. Stephenson, Jr.,** V.A. Hospital, Swannanoa.
 Isaac M. Taylor, N. C. Memorial Hosp., Chapel Hill.
 Oscar A. Thorup, Jr.,* 24 C. Glen Lennox, Chapel Hill.
 James V. Warren, Duke Univ. Med. School, Durham.
 Louis G. Welt, U. of N. C. School of Med., Chapel Hill.
 Ernest H. Yount, Bowman Gray School of Med., Winston-Salem.

NORTH DAKOTA

William E. Cornatzer, U. of N. D. Med. School, Grand Forks.

OHIO

William E. Abbott, Univ. Hosps., 2065 Adelbert Rd., Cleveland.
 Joseph P. Abraham, Cincinnati General Hosp., Cincinnati 29.
 Charles V. Adair, 1010 Woodland Rd., Mansfield.
 Basil D. Anagnost,** 123 17 St., Toledo 2.
 Nina A. Anderson,** 293 S. Washington Blvd., Hamilton.
 N. S. Assali, Cincinnati General Hosp., Cincinnati.
 Albert W. Barile, 4100 W. Third St., Dayton.
 Allan C. Barnes,** Ohio Univ., Columbus 10.
 James H. Barr, Jr., 120 E. 225th St., Cleveland.
 John D. Battle, Cleveland Clinic, 2020 E. 93rd St., Cleveland 6.
 Jerome R. Berman, Cincinnati General Hosp., Cincinnati 29.
 David H. Blankenhorn,* 6 Rural Lane, Cincinnati 20.
 Malcolm Block, 210 Fidelity Bldg., Dayton.
 George T. Booth,** 1031 Secor Hotel, Toledo 4.
 Bertha A. Bouroncle, Kinsman Hall, Ohio State U., Columbus.
 Joseph P. Brady,* Holzer Hosp. & Clinic, Gallipolis.
 Charles H. Brown, Cleveland Clinic, 2020 E. 93rd St., Cleveland 6.
 Helen R. Cash,* 24815 Lakeview Dr., Bay Village.
 Edward M. Chester, 10 Beech, Berea.
 Austin Chinn,** Univ. Hosps., Cleveland.
 Thomas E. Clark, 9 Buttles Ave., Columbus 8.

- Oscar W. Clarke,* Gallipolis Hosp., Box 240, Gallipolis.
- Frederick S. Coombs, Jr.,** 803 Home Savings & Loan Bldg., Youngstown.
- W. Clark Cooper, 1014 Broadway, Cincinnati 2.
- Arthur C. Corcoran,** Cleveland Clinic Found., Euclid at 93rd St., Cleveland 6.
- Sanford R. Courter, 6426 Ridge Ave., Cincinnati.
- James W. Craig, Lakeside Hosp., Cleveland 6.
- John Davis,* 124 S. St. Clair St., Painesville.
- C. Joseph De Lor,** 2074 Arlington Ave., Columbus 8.
- Victor G. De Wolfe, Cleveland Clinic, 2020 E. 93rd St., Cleveland 6.
- John H. Dingle,** School of Med., Western Reserve U., Cleveland 6.
- Matthew C. Dodd,** Dept. of Bact., Ohio State U., Columbus.
- Henry W. Drygas,* 401 Broadway Bldg., Lorain.
- Harriet P. Dustan, Cleveland Clinic Found., Cleveland 6.
- Philip Edlin, 641 Woodside Hgts., Cincinnati 29.
- John T. Flynn, Western Reserve U. Med. School, Cleveland.
- Charles H. Foertmeyer,* 926 Reilly Rd., Wyoming 15.
- Harold S. Ginsberg, Western Reserve U. Med. School, Cleveland 6.
- Edmond F. Glow,** 3118 Kenwood Blvd., Toledo 6.
- Richard E. Goldsmith,* Cincinnati General Hosp., Cincinnati.
- Arnoldus Goudsmith,** 2218 Market St., Youngstown 7.
- Norman E. Goulder, 41 S. Grant Ave., Columbus 15.
- Mervin E. Green, 237 Michigan St., Toledo.
- Robert S. Green, Cincinnati General Hosp., Cincinnati 29.
- Charles G. Guttas,* 2156 St. James Pkwy., Cleveland.
- Donald B. Hackel, 4373 W. 66th St., Cleveland 9.
- Edward O. Hahn, 21535 Lorain Rd., Cleveland 26.
- William H. Hallaran,** 9925 Lake Shore Blvd., Cleveland 8.
- Thomas Hale Ham,** Western Reserve U. Med. School, 2109 Adelbert Rd., Cleveland 6.
- George J. Hamwi, Univ. Hosp., Columbus 10.
- Frank R. Hanrahan, Jr., 407 Osborn Bldg., Cleveland 15.
- John W. Harris, 2176 Edgewood Rd., Cleveland Heights 18.
- Robert W. Heinle,** 2065 Adelbert Rd., Cleveland 6.
- James S. Hewlett, Cleveland Clinic, 2020 E. 93rd St., Cleveland 6.
- John F. Hillabrand,** 212 Colton Bldg., Toledo 2.
- Richard G. Hodges,** Western Reserve U. Med. School, Cleveland 6.
- John H. Holzaepfel, Univ. Hosp., Columbus.
- Theron L. Hopple,* 206 Capistrano, Toledo 12.
- Richard Hotz,** 421 Michigan St., Toledo.
- Charles L. Hudson, 2102 Abington Rd., Cleveland 8.
- Bradley Hull, 15644 Madison Ave., Lakewood.
- Arnold Iglaue,** 1257 Oberlin Blvd., Cincinnati 29.
- Scott R. Inkley, 2102 Abington Rd., Cleveland 6.
- Thomas Jarrold,* Brown Hosp., V.A. Cntr., Dayton.
- William M. Jefferies, 1272 Gene-see Ave., Mayfield Heights 24.
- Philip C. Johnson,* 2211 Tabor Ave., Dayton 10.
- William S. Jordan, 2109 Adelbert Rd., Cleveland.
- Frederick T. Kapp, General Hosp., Cincinnati 29.
- R. W. Kissane,** 9 Buttles Ave., Columbus 8.
- Jerome Kleinerman, 3441 Ashby Rd., Shaker Heights.
- Edward M. Kline,** 10515 Carnegie Ave., Cleveland.
- Ruth A. Koons,** 9 Buttles Ave., Columbus 8.
- Richard A. Leahy,* 170 Noble, Tiffin.
- Stanley Levey, Univ. Hosps., 2065 Adelbert Rd., Cleveland 6.
- Erwin Levin,* 1100 Keith Bldg., Cleveland 15.
- Bennett Levine, Lakeside Hosp., 2065 Adelbert Rd., Cleveland 6.
- Leonard L. Lovshin, Cleveland Clinic, 2020 E. 93rd St., Cleveland 6.
- Kenneth D. Lowry,** 119 S. Mulberry St., Troy.
- Hubert F. Loyke, 1596 E. 82nd St., Cleveland.
- E. Perry McCullagh,** Cleveland Clinic, Cleveland.
- Samuel N. Maimon,** Reibold Bldg., Dayton 2.
- Max Miller,** 2065 Adelbert Rd., Cleveland.
- I. Arthur Mirsky,** May Inst. for Med. Rsrch., Jewish Hosp., Cincinnati.
- John F. Mueller, Cincinnati General Hosp., Cincinnati 29.
- Richard P. Mueller, 1575 Arthur Ave., Lakewood.
- William G. Myers,** 2724 Wexford Rd., Columbus 12.
- Arthur D. Nichol,** 10515 Carnegie Ave., Cleveland.
- Don C. Nouse,* 232 Michigan St., Toledo 2.
- J. E. Owens, 3886 Rocky River Dr., Cleveland.
- Irvine H. Page,** Cleveland Clinic, 2040 E. 93rd St., Cleveland 6.
- Solomon Papper,* 3935 Warwick Ave., Cincinnati.
- Lester Persky, 2065 Adelbert Rd., Cleveland.
- Lawrence Peters, Western Reserve U. Med. School, Cleveland 6.
- Raymond C. Pogge, Wm. S. Merrill Co., Cincinnati 15.
- Noreen G. B. Price, 313 W. 6th Ave., Columbus.
- John A. Prior, Univ. Hosp., Ohio State U., Columbus.
- Charles H. Rammelkamp,** 2109 Adelbert Rd., Cleveland 6.
- Frank F. A. Rawling,** 316 Michigan St., Toledo.
- Roberts M. Rees, Second National Bldg., Akron 8.
- Irving Rothchild, Ohio State U. Coll. of Med., Columbus.
- A. Ashley Rousuck,** 836 Rose Bldg., Cleveland 15.
- Edward Rubenstein,* 830 E. Mitchell Ave., Cincinnati 29.
- George H. Ruggy,** Hamilton Hall, Ohio State U., Columbus 10.
- Joseph M. Ryan,* Univ. Hosp., Ohio State U., Columbus.
- Salvatore M. Sancetta, Cleveland City Hosp., Cleveland.
- Albert Sapadin,* 2003 Auburn Ave., Cincinnati 19.
- Arthur L. Scherbel, Cleveland Clinic, 2020 E. 93rd St., Cleveland 6.
- James F. Schieve, 441 Arden Rd., Columbus 14.
- Adolph B. Schneider, Jr.,* 10515 Carnegie Ave., Cleveland.
- Robert W. Schneider, Cleveland Clinic, Cleveland 6.
- Maurice A. Schnitker,** 1031 Secor Hotel Bldg., Jefferson at Superior, Toledo 4.
- Mary L. Scholl, 1384 Grandview Ave., Columbus 12.
- Albert W. Schreiner,* Cincinnati General Hosp., Cincinnati 29.
- W. B. Seymour,** 2102 Abington Rd., Cleveland 6.
- Nathan Shapiro, 711 Doctors Bldg., Cincinnati.
- Robert S. Shelton,** 6660 Mariemont Ave., Cincinnati 27.
- E. Vernon Smith,* Doctors Bldg., 2508 Auburn Ave., Cincinnati 19.
- Edna H. Sobel, Children's Hosp., Cincinnati.
- Murill M. Szucs,** 800 Dollar Bank Bldg., Youngstown 3.
- Robert D. Taylor, Cleveland Clinic, Euclid Ave. at 93rd St., Cleveland 6.
- Gordon M. Todd, 1035 Secor Hotel Bldg., Toledo 4.
- Joseph F. Tomashefski, Ohio Tuberculosis Hosp., Ohio State U., Columbus 10.
- Thomas E. Twitchell, 4510 Leasher Dr., Dayton 9.

Howard S. Van Ordstrand,** 2020 E. 93rd St., Cleveland.
 Robert L. Wall,* Kinsman Hall, Ohio State U., Columbus.
 Austin S. Weisberger, Lakeside Hosp., Cleveland.
 Richard N. Westcott,* 2020 E. 93rd St., Cleveland 6.
 Claude-Starr Wright, Dept. of Med. Rsrch., Ohio State U., Columbus.
 Arthur F. Young, 15648 Madison Ave., Lakewood.
 Henry A. Zimmerman, 250 Hanna Bldg., Cleveland 15.

OKLAHOMA

Robert H. Bayley,** Univ. of Okla. Med. School, Oklahoma City.
 Robert Bird, Univ. Hosps., 800 N.E. 13th St., Oklahoma City 4.
 John P. Colmore, Univ. Hosps., 800 N.E. 13th St., Oklahoma City.
 Loyal L. Conrad,* Okla. Med. Rsrch. Found., Oklahoma City 4.
 Leonard P. Eitel, 825 N.E. 13th St., Oklahoma City 4.
 Robert H. Furman, Okla. Med. Rsrch. Inst., Oklahoma City.
 R. Palmer Howard, Okla. Med. Res. Inst. Hosp., 825 N.E. 13th St., Oklahoma City.
 Ceylon S. Lewis, Jr., 1526 S. Yorktown, Tulsa.
 Robert C. Lowe,** U. of Okla. School of Med., Oklahoma City 4.
 Reynold Patzer,** U. of Okla. School of Med., 800 N.E. 13th St., Oklahoma City 4.
 Edward C. Reifenshtein, Jr., 1126 Hemstead Pl., Oklahoma City 6.
 Robert A. Schneider, Univ. Hosps., 800 N.E. 13th St., Oklahoma City 4.
 Stewart Wolf, Univ. Hosps., 800 N.E. 13th St., Oklahoma City 4.

OREGON

Russell J. Alleman, 4212 N.E. Broadway, Portland.
 Howard E. Allen, 1216 S.W. Yamhill St., Portland.
 H. R. Allumbaugh,** Medical Center, Eugene.
 Kurt W. Aumann, 249 N. 31st St., Corvallis.
 Russel Baker,** 1020 S.W. Taylor, Portland.
 James W. Bickie,* St. Vincent's Hosp., Portland.
 John D. Bonzer,* 612 Medical Center, Eugene.
 George A. Boylston, 1216 S.W. Yamhill, Portland.
 William M. Burget,* Spexarth Bldg., Astoria.
 Charles S. Campbell,** 1970 Virginia St., Salem.
 Ray L. Casterline, 906 E. Main St., Medford.

William Cohen,** 539 Medical Arts Bldg., Portland.
 Robert J. Condon, 303 Jackson Tower, Portland 5.
 William S. Conklin,** 1006 Standard Insurance Bldg., Portland 5.
 Rudolph M. Crommelin,** 1008 Selling Bldg., Portland.
 Robert L. Cutter,* 1036 Wall, Bend.
 Norman A. David,** Univ. of Ore. Med. School, Portland 1.
 Kenneth B. Davison,** Univ. of Ore. Med. School, Portland 1.
 Samuel M. Diack,** 1216 S.W. Yamhill St., Portland 5.
 H. Lenox H. Dick,* Medical Dental Bldg., Portland.
 Charles T. Dotter, 4004 S.W. Greenleaf Dr., Portland.
 J. E. Field,* 6485 W. Burlingame Pl., Portland.
 Dwight H. Findlay,** 301 Fluhrer Bldg., Medford.
 Elsworth L. Gardner,** 710 Medical Center, Eugene.
 Martin F. Gilmore,* 812 S.W. Washington St., Portland 5.
 Morton J. Goodman,** 2455 N.W. Marshall, Portland 10.
 Jarvis Gould, 3181 S.W. Sam Jackson Pk. Rd., Portland 1.
 Hance F. Haney,** Univ. of Ore. Med. School, Portland 1.
 Bernard P. Harpole,* 711 Selling Bldg., Portland 5.
 Gerald Harpole,* 711 Selling Bldg., Portland 5.
 Harmon T. Harvey, 906 Livesley Bldg., Salem.
 Carl H. Heller,** Univ. of Or., Dept. of Med., Portland.
 Max W. Hemingway,** 1036 Wall St., Bend.
 Blair J. Henningsgaard,* 250 12th St., Astoria.
 Oscar T. Heyerman,* Medical Center Bldg., Medford.
 Ralph E. Hibbs, 1032 W. Main, Medford.
 Jules Hirsch,* U. S. Pub. Health Serv., 220 U. S. Court House Portland 5.
 Marcus Horenstein,* 2719 N.E. 7th Ave., Portland 12.
 William W. Hurst, 908 S.W. Cheltenham St., Portland 1.
 Huldric Kammer, Suite #2, 2455 N.W. Marshall St., Portland 10.
 Roger H. Keane,** 624 Mayer Building, Portland.
 John J. Krygier, 812 S.W. Washington, Portland.
 Richard J. Kulasavage, 7218 N. E. Sandy Blvd., Portland.
 Daniel H. Labby, 5931 S.W. Hamilton St., Portland 1.
 Stuart M. Lancefield,* 110 E. Superior St., Salem.
 Virgil C. Larson,** 1162 Willamette St., Eugene.
 Lawrence D. Leslie,** 1162 Willamette St., Eugene.

Howard P. Lewis,** 3181 S.W. Sam Jackson Pk. Rd., Portland 1.
 William L. Liddbeck,** Livesley Building, Salem.
 Aarne J. Lindgren, 1216 S.W. Yamhill St., Portland.
 L. A. Lodmell,** 1108 Standard Insurance Bldg., Portland.
 George B. Long, 812 S.W. Washington, Portland 5.
 Theodore M. Lundy,** Eugene Clinic, Eugene.
 Elton L. McCawley, 1860 N.E. 66th Ave., Portland 13.
 Guy R. McCutchan,** 7516 N.E. Sacramento, Portland 13.
 John D. McGovern,* 624 Mayer Building, Portland 5.
 Raymond A. McMahon,** 414 Medical-Dental Bldg., Portland 5.
 Barney Malbin,** Medical Arts Bldg., 10th & Taylor, Portland.
 Leo J. Meinberg,** 514 Mayer Building, Portland.
 Fred N. Miller,** University of Oregon, Eugene.
 Robert F. Miller,** 812 N.W. Washington St., Portland 5.
 William R. Miller,* Medical Center, Eugene.
 Philip L. Nudelman,* 311 Mayer Building, Portland.
 Edwin E. Osgood,** Univ. of Ore. Med. School, Portland.
 William C. Pantan,** Medical Arts Building, Portland.
 Joseph F. Paquet,* 2455 N.W. Marshall St., Portland.
 James G. Perkins, 8217 S.W. 19th, Portland 19.
 Frank Perlman,** 406 Medical-Dental Bldg., Portland 5.
 John M. Pierson, 919 Taylor St. Bldg., Portland 5.
 Gordon Prewitt,* 1216 S.W. Yamhill St., Portland 5.
 Clyde J. Rademacher,** 1036 Wall St., Bend.
 Noel B. Rawls, Astoria Clinic, Astoria.
 Leon F. Ray,** 628 Medical-Dental Bldg., Portland 5.
 Charles E. Reed, Corvallis Clinic, Corvallis.
 Demetrios A. Rigas, Univ. of Ore. Med. School, Portland.
 James A. Riley, Rennie Building, Corvallis.
 Arthur L. Rogers,** 1216 S.W. Yamhill St., Portland 5.
 Edward E. Rosenbaum, 4444 S.W. Fairhaven Dr., Portland 1.
 Harold O. Schneider,** 708 Livesley Building, Salem.
 Marvin Schwartz, 3021 N.W. Greenbriar Terrace, Portland.
 William C. Scott, 4212 E. Broadway, Portland 13.
 Arthur J. Seaman, Univ. of Ore. Med. School, Portland 1.
 Philip Selling,* 1216 S.W. Yamhill, Portland.
 Bernard R. Sharff,* Enterprise.

John H. Stalnaker,* 919 S.W. Taylor St., Portland 5.
 Franz R. Stenzel,** 2455 N.W. Marshall, Portland.
 Jon V. Straumfjord,** 348 Commercial St., Astoria.
 Nicholas P. Sullivan,** 832 Medical Center Bldg., Eugene.
 Merle H. Swansen,** 921 Main St., Klamath Falls.
 David K. Taylor,** 1753 N. Wheeler Ave., Portland 12.
 Harold Tivey,* Univ. of Ore. Med. School, Portland 1.
 Joseph B. Trainer, 1127 S.W. Gaines Rd., Portland 1.
 Ben Vidgoff,** 919 S.W. Taylor St., Portland.
 M. L. Vorheis,* Wheeler.
 I. G. Voth,* Medical Arts Building, Portland.
 John D. Welch,* 303 Jackson Tower, Portland 5.

PENNSYLVANIA

Fred Alexander, 125 Old Gulph Rd., Wynnewood.
 Howard N. Baier, 3401 N. Broad St., Philadelphia.
 Mary L. Bailey, Virus Rsrch. Lab., U. of Pitts., Pittsburgh 13.
 William R. Bailey, Jr., Mercy Hospital, Pittsburgh 19.
 Earl S. Barker, Hosp. of the U. of Pa., 706 Maloney Bldg., Philadelphia 4.
 William C. Beck,** Guthrie Clinic, Robert Packer Hosp., Sayre.
 Samuel Bellet,** 2021 Spruce St., Philadelphia.
 Carmen T. Bello, 2502 S. 22nd St., Philadelphia 45.
 J. Edward Berk,** 101 S. 20th St., Philadelphia 3.
 Bernard H. Berman, 331 Washington Trust Bldg., Washington.
 Lewis W. Bluemle, Jr., 303 S. 39th St., Philadelphia 4.
 William P. Boger, 640 N. Broad St., Philadelphia.
 Mark M. Bracken,** Mercy Hosp., Pride & Locust Sts., Pittsburgh.
 William R. Brink, 610 W. 4th St., Williamsport.
 Frank P. Brooks, Hosp. of the U. of Pa., 3400 Spruce St., Philadelphia 4.
 Arthur E. Brown, Jr.,* 317 N. 25th St., Camp Hill.
 William N. Campbell, 3400 N. Broad St., Philadelphia 40.
 Bruce F. Chandler, 711 High St., Honesdale.
 Robert Charr,** 2038 Locust St., Philadelphia 3.
 Francis S. Cheever,** U. of Pitts. School of Pub. Health, Pittsburgh 13.
 John K. Clark, University Hospital, Philadelphia.
 Adolph J. Creskoff,** 107 Long Ave., Upper Darby.
 Alvin J. Cummins, Hosp. of the U. of Pa., Philadelphia 4.

David K. Detweiler, 48 N. Sproul Rd., Broomall.
 Wilton A. Doane,* Oak St., Trucksville.
 Thomas M. Durant,** 3401 N. Broad St., Philadelphia.
 Wallace W. Dyer,** 2016 Delancey St., Philadelphia 3.
 George E. Farrar, Jr.,** Wyeth, 1600 Arch St., Philadelphia 3.
 Ferdinand Fetter,** 322 S. 21st St., Philadelphia.
 Albert J. Finestone, 246 W. Upsal St., Philadelphia 19.
 Peter Fisher, Guthrie Clinic, Robert Packer Hosp., Sayre.
 Harrison F. Flippin,** 255 S. 17th St., Philadelphia 3.
 Robert E. Forster, II, 721 Millbrook Lane, Haverford.
 Abraham M. Frumin, 255 S. 17th St., Philadelphia 3.
 Louis T. Gabriel, Jr., 941 Hamilton St., Allentown.
 I. W. Ginsburg,** 139 Henley Rd., Overbrook Hills, Philadelphia 31.
 Lincoln Godfrey, Jr., 255 S. 17th St., Philadelphia.
 Harry Goldberg, Hahnemann Med. Coll. & Hosp., 230 N. Broad St., Philadelphia.
 Benjamin A. Gouley,** 1614 Locust St., Philadelphia.
 Lawrence Greenman, 125 DeSoto St., Pittsburgh 13.
 Joseph H. Hafkenschiel, Jr., 553 Heath Rd., Merion.
 Robert H. High, 2600 N. Lawrence St., Philadelphia 33.
 Arthur G. Hills, 3400 Spruce St., Philadelphia 4.
 Erwin O. Hirsch, Kelley's Farm, R.D. 2, Phoenixville.
 John M. Hudson,* Pa. Hosp., 8th & Spruce, Philadelphia.
 Harold L. Israel,** 2031 Pine St., Philadelphia.
 Calvin F. Kay, Hosp. of the U. of Pa., 3400 Spruce St., Philadelphia.
 Norman Kendall, 3401 N. Broad St., Philadelphia.
 Richard L. Kendrick, 4815 Larchwood Ave., Philadelphia 43.
 Alfred Kershbaum, 1800 S. 55th St., Philadelphia.
 Morton Klein, Temple U. School of Med., Broad & Ontario Sts., Philadelphia.
 Robert Klein, Children's Hosp. of Pitts., 125 DeSoto St., Pittsburgh.
 H. Roebeling Knoch, 201 Elmwood Blvd., York.
 Norman Learner, Medical Tower, 255 S. 17th St., Philadelphia 3.
 Charles T. Lee, Jr.,* 101 N. Mole St., Philadelphia 2.
 Walter J. Levinsky, 6 B Wissahickon Gardens, Philadelphia 44.
 Mieczyslaw S. Lopusniak, 1817 Windsor Park Lane, Haverford.

Stanley H. Lorber, Fels Rsrch. Inst., Temple U. School of Med., Philadelphia 40.
 Harold A. Lyons, U. S. Naval Hospital, Philadelphia 45.
 Thomas E. Machella,** University Hosp., 3400 Spruce St., Philadelphia.
 Albert G. Marrangoni, Mercy Hosp., 1400 Locust St., Pittsburgh 19.
 Frank M. Mateer, 125 DeSoto St., Pittsburgh 13.
 Solomon S. Mintz, 2422 76th Ave., Philadelphia 38.
 Campbell Moses, 174 Crescent Hill Rd., Pittsburgh 21.
 Ralph M. Myerson, V.A. Hospital, Union & Woodland Aves., Philadelphia.
 Charles M. Norris, 3401 N. Broad St., Philadelphia 40.
 Axel K. Olsen,** 115 Linwood Ave., Ardmore.
 Robert E. Olson, Graduate Sch. of Pub. Hlth. Univ. of Pitts., Pittsburgh.
 Bernard Pastor, 6929 Ardleigh St., Philadelphia 19.
 Raymond Penneys, 2622 Lenape Rd., Philadelphia.
 Irwin J. Pincus, 269 S. 19th St., Philadelphia.
 Edward B. Polin, 5601 N. 16th St., Philadelphia.
 Robert S. Pressman,** 151 W. Grange Ave., Philadelphia 20.
 Edmond Preston, III,* 531 E. Tulpehocken St., Philadelphia 44.
 Fred M. Richardson,** 160 Carpenter Lane, Philadelphia 19.
 Robert Robbins, 1617 West End Dr., Philadelphia.
 James L. d'Aumont Roth, 421 Green Lane, Philadelphia.
 J. Woodrow Savacool,** 146 W. Tulpehocken St., Philadelphia 44.
 John J. Sayen, 506 Montgomery Ave., Haverford.
 Robert C. Schilling,* 3401 N. Broad St., Philadelphia 40.
 Nathan S. Schlezinger,** 255 S. 17th St., Philadelphia 3.
 Truman G. Schnabel, Jr., Hosp. of U. of Pa., 36th & Spruce Sts., Philadelphia 4.
 Norman G. Schneeberg, 1930 Chestnut St., Philadelphia 3.
 Leon Schwartz,** 8340 Fayette St., Philadelphia 19.
 David Seligson, 4230 Parkside Ave., Philadelphia 4.
 Paul L. Shallenberger,** Guthrie Clinic, Sayre.
 Harry Shay,** 3400 N. Broad St., Philadelphia 40.
 Charles R. Shuman, Temple U. Hosp., Broad & Ontario Sts., Philadelphia 40.
 Andrew Sokalchuk, 14074 Erwin St., Philadelphia.

Louis A. Soloff, ** 255 S. 17th St., Philadelphia.
 Maurice Sones, ** Mount Airy Med. Bldg., Germantown & Mt. Pleasant Ave., Philadelphia.
 Russell D. Squires, 402 N. Springfield Ave., Clifton Heights.
 Herbert M. Stauffer, * 3401 N. Broad St., Philadelphia 40
 Howard H. Steel, Manheim Gardens, Philadelphia.
 William A. Steiger, 3432 N. Broad St., Philadelphia 40.
 Aaron H. Stock, ** Children's Hosp. of Pitts., 125 DeSoto St., Pittsburgh.
 T. R. Talbot, Jr., Hosp. of the U. of Pa., 3400 Spruce St., Philadelphia 4.
 Robert Tarall, 125 DeSoto St., Pittsburgh 13.
 John Tredway, 233 West 8th St., Erie.
 Howard D. Trimpi, 255 S. 17th St., Philadelphia 3.
 Ralph R. Tyson, Temple U. Hosp., Philadelphia.
 Victor C. Vaughan, III, 2600 N. Lawrence St., Philadelphia 33.
 Jerome M. Waldron, Temple U. School of Med., 3400 Broad St., Philadelphia 40.
 Richard L. Wechsler, 2134 Mather Way, Philadelphia.
 William Weiss, 445 E. Slocum St., Philadelphia 19.
 Jack W. Welty, ** Owen Rd. & Montgomery Ave., Wynnewood.
 Martin Wendkos, ** 4015 Baltimore Ave., Philadelphia 4.
 C. Wilmer Wirts, Jr., ** 2017 Delancey Pl., Philadelphia.
 John R. Wolgainot, * Pa. Hosp., 8th & Spruce, Philadelphia.
 Henry T. Wycis, ** Temple U. Hosp., Philadelphia 40.
 Chris J. D. Zarafonitis, Temple U. Med. School, Philadelphia.
 Jacob Zatuschni, 735 E. Upsal St., Philadelphia.
 William W. Zeller, 4111 Berry Ave., Drexel Hill.
 Harry F. Zinsser, Jr., Hosp. of the U. of Pa., 36th & Spruce Sts., Philadelphia 4.

RHODE ISLAND

Francis H. Chafee, ** 154 Waterman St., Providence.
 Frank B. Cutts, ** 154 Waterman St., Providence 6.

SOUTH CAROLINA

W. J. Butt, ** 6212 Woodlawn Ave., Box 82, Columbia.
 Richard M. Christian, 514 Hodges Bldg., Greenwood.
 William R. Craig, Jr., * 210 E. Coffee St., Greenville.
 Peter C. Gazes, 696 Rutledge Ave., Charleston.
 Franklin L. Geiger, ** 3907 Fernholm Rd., Columbia.

Myers H. Hicks, 315 S. Coit, Florence.
 G. R. Hodge, 3 Catawba St., Spartanburg.
 Frederick W. Kinard, ** U. of S. C. Med. Coll., Charleston 16.
 Clarence W. Legerton, Jr., Conway.
 Karl M. Lippert, ** V.A. Hospital, Columbia.
 William M. McCord, ** Medical College, Charleston 16.
 Vince Moseley, Med. Coll. of the State of S. C., Charleston.
 James A. Richardson, Medical College of S. C., Charleston 16.
 Paul Kent Switzer, Union.
 Solomon Zimmerman, V.A. Hospital, Columbia.

TENNESSEE

Ben J. Alper, * 3011 Fox Dr., Chattanooga 4.
 William L. Alsobrook, 5573 Knob Rd., Nashville 9.
 Allan D. Bass, ** Vanderbilt Med. School, Nashville 5.
 Frederic T. Billings, Jr., Vanderbilt U. Hosp., Nashville.
 Thos. M. Blake, Vanderbilt U. Hosp., Nashville 4.
 George B. Brothers, Meharry Med. Coll., Nashville 8.
 Landry E. Burgess, ** Meharry Med. Coll., Nashville 8.
 Benjamin F. Byrd, 2122 West End Ave., Nashville.
 Ralph J. Cazort, Meharry Med. Coll., Nashville 8.
 James E. Cottrell, ** Kennedy Veterans Hosp., Memphis 15.
 Orrie A. Couch, Jr., 2122 West End Ave., Nashville.
 Frederic E. Cowden, 1018 Bennie Dillon Bldg., Nashville.
 E. Perry Crump, ** Meharry Med. Coll., Nashville 8.
 William J. Darby, Vanderbilt U. School of Med., Nashville.
 Floyd W. Denny, * Vanderbilt U. Hosp., Nashville.
 Wolcott B. Dunham, ** V.A. Med. Tchng. Grp., Kennedy Hosp., Memphis 15.
 Robert M. Finks, ** 2122 West End Ave., Nashville.
 Benjamin R. Gendel, ** Kennedy Veterans Hosp., Memphis 15.
 Robert A. Goodwin, Jr., Thayer Hospital, Nashville.
 Paul F. Hahn, ** Cancer Research Labs., Meharry Med. Coll., Nashville 8.
 Aubrey B. Harwell, 2122 West End Ave., Nashville.
 Charles W. Johnson, Meharry Med. Coll., Nashville.
 Thomas W. Johnson, Meharry Medical Coll., Nashville.
 J. Allen Kennedy, ** 910 Bennie Dillon Bldg., Nashville.
 Frederick H. Knox, Jr., * Box 47, Kennedy V.A. Hosp., Memphis 15.

Ross C. Kory, 1219 Lone Oak Rd., Nashville.
 Alfred P. Kraus, Dept. of Med. Labs., U. of Tenn., Memphis.
 Roy S. Leadingham, ** V.A. Hospital, Murfreesboro.
 Aaron M. Lefkovits, ** 3200 Union Ave., Extd., Memphis.
 Rudolph A. Light, ** Vanderbilt U. Hosp., Nashville.
 Donald H. McGlory, * Chem. Dept., Vanderbilt U., Nashville.
 George R. Meneely, ** Thayer V.A. Hosp., Nashville.
 H. C. Meng, Vanderbilt Med. School, Nashville 4.
 J. Pervis Milnor, Jr., 1412 Madison Ave., Memphis.
 E. White Patton, 301 Interstate Bldg., Chattanooga.
 Marion L. Patton, ** 1753 Gallo-way Ave., Memphis.
 Cyril Peterson, ** Vanderbilt School of Med., Nashville.
 Samuel Phillips, ** Box 15, Kennedy Hosp., Memphis.
 Gerald I. Pittman, Kennedy V. A. Hosp., Memphis 15.
 Robert L. Post, 6310 Vanderbilt Med. School, Nashville 4.
 William H. Reeder, Medical Arts Bldg., Knoxville.
 Dan C. Roehm, V.A. Hospital, Nashville.
 Luther E. Smith, Donelson.
 Mildred T. Stahlman, Lynwood Blvd., Nashville.
 R. T. Terry, ** Thayer V.A. Hosp., Nashville 5.
 Odon F. von Werssowetz, ** Thayer V.A. Hosp., Nashville.
 Matthew Walker, ** Meharry Med. College, Nashville.
 Albert Weinstein, ** 412 Doctors Bldg., Nashville 3.
 Harold D. West, ** 2426 Jefferson St., Nashville.
 Clarence C. Woodcock, * Thayer Hospital, Nashville.
 Clarence W. Wright, Meharry Med. Coll., Nashville.

TEXAS

Harry Carnes, ** 5119 Bellaire Blvd., Bellaire.
 Don W. Chapman, Baylor U. Coll. of Med., Box 156, Houston.
 Edward W. Dennis, Baylor U. School of Med., Houston.
 Alvan G. Foraker, M. D. Anderson Hosp., 2310 Baldwin St., Houston 6.
 Ralph Vernon Ford, 3907 Daphne, Houston 21.
 Alfred W. Harris, ** Gaston Ave. Med. Bldg., 3607 Gaston Ave., Dallas.
 Haynes Harvill, 302 Medical Arts Bldg., Dallas 1.
 Robert A. Hettig, ** Dept. of Int. Med., Baylor U., Houston.
 Howard E. Heyer, ** 2211 Oak Lawn Ave., Dallas.

Vincent Hollander, Randolph Village, Randolph Air Force Base, San Antonio.
 Daniel E. Jenkins, Baylor U. Coll. of Med., Houston.
 Robert L. Johnson,* 3750th Med. Grp., Sheppard AFB, Wichita Falls.
 Frank J. Kelly, 3746 Merrick Dr., Houston.
 William C. Levin, U. of Texas Med. School, Galveston.
 Leonard L. Madison, Southwestern Med. School of the U. of Texas, Dallas.
 Lawrence G. May, U. of Texas Med. Branch, Galveston.
 Matthew H. Metz,** 4319 Oak Lawn Ave., Dallas.
 John H. Moyer, Baylor U. School of Med., Houston.
 Ralph A. Murphy, Jr., 15 Cynthia Lane, Denison.
 Fitzhugh C. Pannill, Jr., Baylor U. Coll. of Med., Houston 5.
 Paul B. Reaser,* Box 2003, Tyler.
 Lawrence R. Rodgers,* 5000 Montrose Blvd., Houston.
 Arthur Ruskin,** U. of Texas, Med. Branch, Galveston.
 Sidney Schnur,** 411 Medical Arts Bldg., Houston 2.
 Donald W. Seldin, S.W. Med. School of U. of Texas, 2211 Oak Lawn Ave., Dallas.
 Alvin P. Shapiro,* S.W. Med. School of U. of Texas, Dallas.
 Ray H. Skaggs, 4247 Sunset Blvd., Houston 5.
 Charles L. Spurr, 2002 Holcombe Blvd., Houston.
 Elias Strauss, 3614 Fairmount, Dallas 4.
 Ephraim Wagner, 4109 Montrose Blvd., Houston.
 Robert A. Wise,** Box 2180, Houston.
 Ellard M. Yow, 3911 Norfolk St., Houston.

UTAH

Harold Brown, Veterans Hosp., Salt Lake City 3.
 Merrill C. Daines,* 420 E. 10th N., Logan.
 Jean H. Dougherty,* 1872 Princeton Ave., Salt Lake City.
 Arthur B. French, Coll. of Med., U. of Utah, Salt Lake City 1.
 Louis S. Goodman,** 1209 E. 4th St., Salt Lake City.
 Hans H. Hecht, Dept. of Med., U. of Utah, 2033 S. Lake St., Salt Lake City 5.
 B. V. Jager, Salt Lake City General Hosp., Salt Lake City 5.
 James M. Kimball,** 907 Connor St., Salt Lake City.
 Charles W. Sorenson, U. of Utah Med. School, Salt Lake City.
 Frank H. Tyler, 175 E. 21st St., Salt Lake City.
 Maxwell M. Wintrobe,** 175 E. 21st South St., Salt Lake City 15.

VERMONT

Ellsworth L. Amidon,** 144 De Forest Rd., Burlington.
 John H. Bland, 343 S. Prospect St., Burlington.
 Laura Brooks,* Box 168, Bennington.
 Robert G. Gale,* The Fitch Clinic, 122 Railroad St., St. Johnsbury.
 Richard H. Saunders, Jr., Mary Fletcher Hosp., Burlington.
 Ethan Sims, U. of Vt. Coll. of Med., Burlington.
 Andrew Yeomans,** Veterans Hospital, White River Junction.

VIRGINIA

William M. Anderson,* 1604 Grove Ave., Richmond.
 James P. Baker, U. of Virginia Hosp., Charlottesville.
 Richard C. Bentinck, 4313 32nd Rd., S., Fairlington, Arlington.
 James O. Burke, 1200 E. Broad St., Richmond.
 Kenneth Crispell, U. of Virginia Dept. of Med., Charlottesville.
 Charles Crockett, Jr., 920 S. Jefferson St., Roanoke 16.
 Robert K. Davis,* 908 Biscayne Dr., Alexandria.
 Milton Ende, 8 Marshall St., Petersburg.
 Alto E. Feller,** U. of Virginia School of Med., Charlottesville.
 Lester I. Fox,* 94 Ingalls Rd., U. S. Army Hosp., Fort Monroe.
 Stanley Green, 1415 N. Taft St., Arlington 1.
 John L. Guerrant,** U. of Virginia Hosp., Charlottesville.
 G. Watson James, III, Med. Coll. of Virginia, Richmond.
 Ben G. Jones, Jr., 121 N. Washington St., Alexandria.
 Herbert G. Langford,* Med. Coll. of Virginia, Richmond.
 Alferd H. Lawton, Aero Meadows, Route 3, Hernon.
 Byrd S. Leavell,** U. of Virginia Hosp., Charlottesville.
 Bernard Lidman,** 621 Wainwright Bldg., Norfolk.
 John H. McClung,* 113 White, Lexington.
 William W. McClure, 3315 W. Franklin St., Richmond 21.
 Herman M. Nachman,* 1200 E. Marshall St., Med. Coll. of Virginia, Richmond 19.
 James A. Orbison, U. S. Army Hosp., Fort Belvoir.
 Ralph C. Parker, Jr.,** U. S. Naval Hosp., Portsmouth.
 Alvin E. Parrish, 3706 S. 12th St., Arlington.
 William Parson, U. of Va., Dept. of Int. Med., Univ. Station, Charlottesville.
 Philip Young Paterson, Dept. of Microbiology, Univ. of Virginia School of Medicine, Charlottesville.

John L. Patterson, Dept. of Med., Med. Coll. of Va., Richmond 19.
 Herbert R. Pearsall, 818 Orchard Hill, S.E., Roanoke.
 Kemp Plummer,* V.A. Hospital, Richmond.
 Reno R. Porter,** Med. Coll. Hosp., Richmond.
 T. C. Prentice, 1522 Dogwood Dr., Alexandria.
 John C. Ransmeier, 1004 Valley Dr., Alexandria.
 Donald Shotton, 719 Church St., Lynchburg.
 Elam C. Toone, Jr.,** Med. Coll. of Virginia, 1200 E. Broad St., Richmond.
 Henry St. George Tucker, Jr., Med. Coll. of Virginia Hosp., Richmond.
 Gilman R. Tyler,** 810 W. Franklin St., Richmond.
 John H. Vaughan, Med. Coll. Hosp., Richmond.
 James G. Watson, III, Med. Coll. of Virginia, Richmond.
 Hyman S. Zfass, 2502 Monument Ave., Richmond.
 Isadore S. Zfass,** 2502 Monument Ave., Richmond 20.

WASHINGTON

Edward W. Abrames,** Paulsen Medical & Dental Bldg., Spokane.
 Russell R. de Alvarez,** U. of Washington Med. School, Seattle 5.
 H. A. Anderson, 402 South 1, Tacoma.
 John L. Bakke, U. of Washington Med. School, Seattle 5.
 James B. Bingham, U. of Washington Med. School, Seattle 5.
 Hugh S. Brown, Paulsen Medical & Dental Bldg., Spokane.
 Floyd M. Burg,* 1114 Boylston, Seattle 1.
 Fred L. Burrows,* 2910 Shelton Ave., Yakima.
 Edmund W. Campbell,* 208 Lester Ave., Yakima.
 Norman C. Chivers, V.A. Hosp., 4435 Beacon Ave., Seattle 8.
 Harvey G. Copsey,* 66 W. 8th Ave., Spokane 9.
 Joseph H. Crampton, 1115 Terry Ave., Seattle 1.
 Joseph H. Delaney,** 66 West 8th, Spokane.
 Kenneth Eather, 2359 Rosemont Pl., Seattle 99.
 Harold M. Engle, Veterans Hospital, Seattle 8.
 Robert S. Evans, V.A. Hosp., 4435 Beacon Ave., Seattle 8.
 Clement A. Finch, U. of Washington Med. School, Seattle 5.
 Jack W. Fleming,* U. S. Army Hosp., Camp Hanford, Richland.
 Thomas B. Gibbons, 1115 Terry Ave., Seattle 1.
 Russell B. Hanford,** 407 W. Riverside Ave., Spokane.

James W. Haviland,** 1022 Summit, Seattle 4.
Edward Heyde,** Medical Arts Building, Vancouver.
 Thomas H. Holmes, U. of Washington Med. School, Seattle 5.
W. F. Holmes,** 217 Baker Building, Walla Walla.
Howard P. Holt, Yakima Clinic, 102 S. Naches, Yakima.
Connie I. Hood,* 917 Larson Bldg., Yakima.
Ralph Huff,* Tacoma Medical Center, Tacoma.
Emil Jobb,* Medical-Dental Bldg., Seattle 1.
Philip E. Kendall, Kadlek Hospital, Richland.
M. F. Kepl, 407 W. Riverside Ave., Spokane 8.
E. O. King,** 120 E. Birch, Walla Walla.
Robert L. King,** 1115 Terry Ave., Seattle 1.
William M. Kirby, U. of Washington Med. School, Seattle 5.
Evrel A. Larson,** Medical-Dental Center, Bellingham.
F. G. LeFor,** 307-319 South 12th Ave., Yakima.
John H. Lehmann,** 5300 Ballard Ave., Seattle 7.
Sol Levy,** Box A, Medical Lake. Arch Logan, Jr., 66 W. 8th Ave., Spokane.
Joseph H. Low,** 102 S. Naches Ave., Yakima.
Frank P. Mathews,** 305 Security Bldg., Olympia.
James M. Mattson,** 1206 S. 11th St., Tacoma.
Jean C. Michel, U. of Washington Med. School, Seattle 5.
Edward H. Morgan, Mason Clinic, 1115 Terry Ave., Seattle.
William N. Myhre,** 407 Riverside Ave., Spokane 8.
O. Charles Olson, 315 Medical Center, Spokane.
Lester J. Palmer,** 1115 Terry Ave., Seattle 1.
Clarence C. Pearson, 1115 Terry Ave., Seattle 1.
Heyes Peterson,* Medical Arts Building, Vancouver.
Randolph P. Pillow, 1115 Terry Ave., Seattle 1.
Fred Plum, U. of Washington Med. School, Seattle.
Charles D. Rehm,* 1114 Boylston Ave., Seattle.
Herbert S. Ripley,** U. of Washington Med. School, Seattle 5.
Ernest Seward, Permanente Hospital, Vancouver.
Robert J. Sayer,* U. of Washington Med. School, Seattle.
Robert W. Simpson, 804 Medical & Dental Bldg., Seattle 1.
John W. Skinner,** 2701 Shelton Ave., Yakima.
James N. Sledge,* 334 Medical Center Bldg., Spokane.
Alexander R. Stevens, Jr., 6548 55th N.E., Seattle 5.

Merritt H. Stiles,** 315 Medical Center Bldg., Spokane 9.
Edward K. Stimpson,** Bellingham.
Carol L. Sundberg,* 231 Medical Center Bldg., Spokane.
Max S. Thomas,* Bldg. 12, Medical Center, Tacoma.
C. P. Wangeman,** Associated Anesthesiologists, 1110 Harvard Avenue, Seattle 22.
Arthur B. Watts,* 103 E. Holly St., Bellingham.
Eliz. Main Welty,* Paulsen Medical-Dental Bldg., Spokane.
James L. Wilson, 3814 E. Lee St. Seattle.
William A. Wolfe, Bellevue Clinic, Bellevue.
Bruce Zimmerman, 902 Boren Ave., Seattle 4.
August G. Zoet,** 1115 State St., Bellingham.

WEST VIRGINIA

Bert Bradford, Jr.,** 603 Atlas Bldg., Charleston.
William T. Hall,* Greenbrier Clinic, White Sulphur Springs.
E. E. Myers,** Philippi.

WISCONSIN

John A. Beyer, 225 Princeton Ave., Madison 5.
John W. Brown,** Dept. of Preventive Medicine, U. of Wisconsin, School of Med., Madison.
Robert T. Capps, McArdle Memorial Bldg., N. Charter St., Madison 6.
Jules Chase, 536 W. Wisconsin Ave., Milwaukee 3.
Archer P. Crosley, Jr., 2500 Overlook Terrace, Madison.
Charles W. Crumpton, State of Wis. General Hosp., 1300 University Ave., Madison 6.
William P. Deiss, Jr., University Houses, Madison 5.
Helen A. Dickie, State of Wis. General Hosp., Madison 6.
Silas M. Evans,** 324 E. Wisconsin Ave., Milwaukee.
Nathan Grossman, 606 W. Wisconsin Ave., Milwaukee 3.
Otto V. Hibma, 110 E. Main St., Madison 5.
George W. Hillard,* 2842 N. 9th St., Milwaukee.
Sture Johnson,** U. of Wis. Med. School, Madison 6.
Thomas H. Lorenz, Wis. General Hosp., 1300 University Ave., Madison.
Mischa J. Lustok, 536 W. Wisconsin Ave., Milwaukee.
Jack F. March,* 413 4th St., Algoma.
Wallace Marshall,** Bank of Two Rivers Bldg., Two Rivers.
Donald W. Rennie,* U. of Wis. Med. School, Madison.

Edward P. Roemer,** Wis. General Hosp., Madison 6.
Francis Rosenbaum, 425 E. Wisconsin Ave., Milwaukee 2.
George G. Rowe, University Hosp., 1300 University Ave., Madison 6.
Robert F. Schilling, Wis. General Hosp., 1300 University Ave., Madison.
J. L. Sims, Wis. General Hosp., Madison 6.
Henry M. Suckle, 414 Tenney Bldg., Madison.
James M. Wilkie, 110 E. Main St., Madison 6.
Gordon Worley, Jr., 1010 Yale Rd., Madison.

WYOMING

Francis J. Catanzaro, Streptococcal Dis. Lab., Warren Air Force Base.
William D. Perry, Streptococcal Dis. Lab., Warren Air Force Base.
Alan C. Siegel, 1616 Western Ave., Warren Heights, Cheyenne.
Chandler A. Stetson, Streptococcal Dis. Lab., Warren Air Force Base, Cheyenne.
Bertrand L. Stolz, Streptococcal Dis. Lab., Warren Air Force Base, Cheyenne.

OUTSIDE OF UNITED STATES

Leyland J. Adams,** 1374 Sherbrooke St. W., Montreal, Canada.
T. W. H. Armitage,** 136 E. 15th St., North Vancouver, B. C., Canada.
Ennio Cosimo Damiao Barbato, Hospital das Clinicas da Faculdade de Medicina de S. Paulo, Sao Paulo, Brazil.
G. Richard R. Bobb, School of Medicine, U. of P. R., San Juan 22, Puerto Rico.
Thomas Wade Burns, Namru #3, % American Embassy, Cairo, Egypt.
John W. Caldwell,** 1701 West Broadway, Vancouver, B. C., Canada.
Ronald D. T. Cape, Metabolic Unit, Vancouver General Hosp., Vancouver, B. C., Canada.
David Christie,** 1004 W. 32nd Ave., Vancouver, B. C., Canada.
E. Christopherson,** 925 Georgia St., Vancouver, B. C., Canada.
W. H. Cockcroft, 5611 Highbury St., Vancouver, B. C., Canada.
Henry R. Cooper, 1421 Alencastre St., Honolulu, T. H.
James Hilton Darragh, 5645 Queen Mary Rd., Montreal 29, Canada.
Luiz V. Decourt,** Rua Jose de Freitas Guimaraes No. 3, Pacamebu, Sao Paulo, Brazil.
John W. L. Doust, Toronto Psychiatric Hosp., 2 Surrey Pl., Toronto, Canada.

- Franklin H. Epstein, 1st General Dispensary, Fort Richardson, Alaska.
- Brock M. Fahrni,* 1665 W. Broadway, Vancouver, B. C., Canada.
- Antonio Fernandez,* Base Hospital, Ramey A.F.B., Puerto Rico.
- Clementino Fraga Filho, Rua Frederico Eyer, 82 Gavea, Rio de Janeiro, Brazil.
- H. V. B. Gale,** 532 West Broadway, Vancouver, B. C., Canada.
- Jacques Genest, Clinical Research Dept., Hotel Dieu Hospital, Montreal, Canada.
- Michele Gerundo,** Guam Memorial Hospital, Guam, M. I.
- Rafael Giannella, Rua Padre Raposo, 141, Sao Paulo, Brazil.
- Michel A. Jamra, Av. Sao Joao, 1151, 9° conj. 92, Sao Paulo, Brazil.
- Pedro Jannini, Rua Piraposa 248, Sao Paulo, Brazil.
- Archie M. Johnson,* 710 Seymour St., Vancouver, B. C., Canada.
- Arthur Hakstian,** 5909 Trafalgar St., Vancouver, B. C., Canada.
- James D. Hatcher, Queens University, Kingston, Ontario, Canada.
- Victor O. Hertzman, 1744 West Broadway, Vancouver, B. C., Canada.
- M. M. Hoffman, Allan Memorial Inst., 1025 Pine Ave. West, Montreal, Quebec, Canada.
- Charles L. Hunt,** 2009 Trutch St., Vancouver, B. C., Canada.
- F. W. B. Hurlburt,* 1701 W. Broadway, Vancouver, B. C., Canada.
- Robert J. Kalthoff, 72nd Medical Group, Ramey Air Force Base, Puerto Rico.
- Paul H. Kepkay,* 1701 W. Broadway, Vancouver, B. C., Canada.
- Robert B. Kerr,** Univ. of British Columbia, % Vancouver General Hosp., Vancouver, B. C., Canada.
- James L. McCallum, 1610 Pine Ave., West, Montreal, Quebec, Canada.
- Keith MacLean,** 1050 W. 27th, Vancouver, B. C., Canada.
- Harry C. McNamara,* 55th Medical Gr., Ramey A.F.B., Puerto Rico.
- Josephine Mallek, 1588 Westbrook Cres., Vancouver, B. C., Canada.
- J. Margulius,** 552 Columbia St., New Westminster, B. C., Canada.
- A. K. Mathisen, 925 W. Georgia, Vancouver, B. C., Canada.
- Emilio Mattar, Alameda Fernao Cardim 371, Sao Paulo, Brazil.
- A. P. Meiklejohn, Dept. of Medicine, Univ. New Buildings, Edinburgh, Scotland.
- Joao Alves Meira,** University of Sao Paulo, Box 99 B, Sao Paulo, Brazil.
- Ernesto Mendes, Rua Angatuba 308, Sao Paulo, Brazil.
- Ernesto Mendes,** Rua Angatuba 308, Sao Paulo, Brazil.
- Philip W. Morse,** 1375 West Broadway, Vancouver, B. C., Canada.
- Bernard B. Moscovich,** 718 Granville, Vancouver, B. C., Canada.
- J. C. Moscovich,** 515 Birks Building, Vancouver, B. C., Canada.
- D. S. Munroe,** 925 W. Georgia, Vancouver, B. C., Canada.
- Bussamara Neme, 691 Alameda Campinas, Sao Paulo, Brazil.
- William J. Osher, Instituto Nacional de Cardiologia, Cuauhtemoc 300, Mexico, D. F.
- Russell A. Palmer,** 925 West Georgia St., Vancouver, B. C., Canada.
- A. W. Perry, 306 Royal Trust Bldg., Victoria, B. C., Canada.
- George A. Pipilis,** Nicodimou 24, Athens, Greece.
- Jose Fernandes Pontes, Rua Martin Francisco 471, 2° andar, Sao Paulo, Brazil.
- Charles S. Rennie,* 1744 West Broadway, Vancouver, B. C., Canada.
- Leonard Ritzman, 98 General Hospital, Munich, Germany.
- P. W. Semenchuk,* 313 Pemberton Bldg., 625 Fort St., Victoria, B. C., Canada.
- Bruce Shallard,** 1734 W. Broadway, Vancouver, B. C., Canada.
- Selichi Shimomura, Atomic Bomb Casualty Commission, Hiji-yama, Hiroshima City, Japan.
- Frank L. Skinner,** 923 Birks Bldg., Vancouver, B. C., Canada.
- Peter Howard Spohn, 1701 West Broadway, Vancouver, B. C., Canada.
- Neil R. Stewart,* 625 Fort St., Victoria, B. C., Canada.
- Bundham Sundharagiatl, 847 Petchburi Rd., Near Pratunam Pathumvan, Bangkok, Thailand.
- Alvin Jerome Thompson, 55th Medical Group, Ramey A.F.B., Puerto Rico.
- Stuart R. Townsend,** 1414 Drummond, Suite 901, Montreal, Quebec, Canada.
- Bernardine Tranchesi,** Rua Araugo 165, 10° Andar, Sao Paulo, Brazil.
- M. Martin Tunis, 3790 Cote St. Catherine Rd., Apt. 18, Montreal, Quebec, Canada.
- S. E. C. Turvey,** 6389 Mac Donald, Vancouver, B. C., Canada.
- Edmundo Vasconcelos,** Caixa Postal 4066, Sao Paulo, Brazil.
- Harris S. Wendorf,** Base Hospital, Ramey A.F.B., Puerto Rico.
- Joseph Wener, 1499 Bishop St., Montreal, Quebec, Canada.
- D. M. Whitelaw,* 5760 Marguerete, Vancouver, B. C., Canada.
- Reginald Wilson,** 2525 Pine St., Vancouver, B. C., Canada.

ADDENDA

CALIFORNIA

Roby J. F. Renshaw,** 1527 N. B'way, Santa Ana.

COLORADO

Stanley B. Crosbie,** VA Hosp., Grand Junction

DISTRICT OF COLUMBIA

Francis J. Murray,* 2111 Bancroft Pl., N.W., Washington.

IDAHO

Charles C. Johnson, 403 Eastman Bldg., Boise.

INDIANA

Raymond M. Rice,** % Eli Lilly Co., Box 618, Indianapolis 6.

MASSACHUSETTS

N. Robert Frank, Heart Sta., Boston City Hosp., Boston.

MICHIGAN

John M. Weller, 1130 Fair Oaks Pkwy., Ann Arbor.

MISSOURI

Bernard A. Bercu, Barnes Hosp., St. Louis.

S. L. Stephenson,* 746 Manship, Jackson.

Don L. Thurston,** St. Louis Children's Hosp., 500 S. Kingshighway, St. Louis 10.

NORTH CAROLINA

Charles E. Kiely, Infirmary, US-MCALF, Edenton.

est
C.,
ral
on
ia,
ad-
da.
mb
iji-
an.
rks
C.,
est
C.,
St.,
847
am
nai-
5th
B.,
um-
ue-
Rua
Sao
St.
ton-
Mac
C.,
Caix
azil.
Hos-
uerto
St.,
la.
rete,
da.
Pine
ada.

osp.,
ship,
Chil-
shigh-

y, US-

Clinical Research Proceedings

Volume I, 1953

INDEXES

Clinical Research Proceedings, Vol. I, 1953

No. 1, APRIL

Abstracts submitted to Sectional meetings of the
American Federation for Clinical Research:
Midwestern Section, Chicago, November 1952,
page 3
Eastern Section, New York, December 1952,
page 13
Western Section, Carmel, Calif., January 1953,
page 26
Southern Section, New Orleans, January 1953,
page 38
Eastern Section, Syracuse, N. Y., December
1951, *page 52*

No. 2, SEPTEMBER

Abstracts submitted to the National Meeting of
the American Federation for Clinical Research,
Atlantic City, May 1953, *page 61*
Notices of Importance to Investigators, *page 118*
Membership Roster, American Federation for
Clinical Research, *page 121*
Annual Author Index, *page 143*
Annual Subject Index, *page 148*

AUTHOR INDEX

Abbott, L. D., Jr., 64
Abbott, W. E., 9
Abelmann, W. H., 17
Adair, C. V., 101
Adlersberg, D., 89
Almy, T. P., 24
Alpert, L. K., 88
Alway, R. H., 27
Anderson, L. L., 6
Angrist, A., 59
Araujo, J., 15
Arons, W. L., 113
Artman, E. L., 47
Ashley, M. M., 31
Atlas, L. T., 92
Axelrod, A., 64

Bagnall, A. W., 35
Bakst, H., 18
Balch, H. E., 36
Ball, C. T., 40
Barger, A. C., 77
Barnes, A. C., 10
Barrett, J. L., 33, 34, 95
Barton, W. B., 114
Bass, D. E., 85
Bateman, J. C., 22, 57
Battley, L. L., 83
Battle, J. D., Jr., 3
Bayne, G. M., 23
Beard, M. F., 3
Beazley, H. L., 38
Bechtold, E., 59
Beckmans, M. L., 61
Beierwaltes, W. H., 10, 95, 96, 115
Belle, M. S., 82
Bellet, S., 83
Benjamin, J. W., 59
Benjamin, Z. H., 18
Bennett, A., 40, 41
Benson, R. H., 113

Berghan, R., 96
Berkman, S., 36
Berk, J. E., 58
Berkowitz, D., 105
Berlin, N. I., 61
Bernfeld, P., 69
Bernstein, S. H., 105
Best, M. M., 50
Bethard, W. F., 26
Bierman, H. R., 69
Billings, F. T., 40
Bisel, H. F., 72
Blair, E., 51
Blake, T. M., 40
Blatt, N. B., 11
Blocker, T. G., Jr., 90
Blount, S. G., Jr., 6, 28
Bobb, J. R. R., 15
Boger, W. P., 23
Boling, J. L., 34, 102
Bond, W. H., 8
Boren, H. G., 47
Boyd, L. J., 65
Bradford, S., 21, 99
Brainard, H., 104
Braude, A. I., 68
Brennan, M. J., 65
Brick, I. B., 110, 112
Brock, L. L., 30
Broida, H. P., 18
Brooks, F. P., 21
Brooks, L., 77
Brooks, M., 68
Brown, E., 28, 29
Brown, H., 93
Brown, W. E., 49
Burch, G. E., 45
Burchenal, J., 51
Burke, J. O., 21, 99
Burnett, C. H., 92
Burnum, J. F., 39

Burrows, B. A., 20, 31, 111
Byron, R. L., 69
Cailoutte, J., 109
Callahan, E. J., III, 78
Camp, J., 88
Campagna-Pinto, Dante, 110
Cantor, J. A., 105
Cappa, R. T., 81
Capps, R. B., 58
Cardon, P. V., 79, 82
Cargill, W. H., 49
Catz, B., 31
Chalmers, T. C., 101
Chandler, D., 56
Chapman, C. B., 7, 76, 79
Chapman, D. W., 38, 41
Chason, W. H., 84
Chatterjea, J. B., 53
Chaudhuri, S. N., 47
Chenoweth, M. B., 98
Chiesky, K., 54
Chiu, G.-C., 56
Chodos, R. B., 111
Chute, R., 25
Cigarroa, J. G., 101
Cintrón-Rivera, A. A., 80
Clark, E. J., 72
Clark, R. G., 55
Clifford, G. O., 6, 63
Coleman, D. H., 66
Commons, R. R., 31, 33, 36
Conrad, H., Jr., 66
Conrad, L. L., 38
Coon, W. W., 3
Coonrad, E. V., 114
Cooper, G. R., 112
Cooper, E. S., 83
Corcoran, A. C., 6
Cordes, F. L., 69
Cornatzner, W. E., 43

- Craig, J. W., 9, 87
 Craige, C. E., 77
 Creticos, A. P., 74
 Crispell, K. R., 44, 45, 88, 91
 Crosby, W., 64
 Crumpton, C. W., 81
 Cummins, A. J., 99

 Dahl, J. C., 7
 Dailey, M. E., 32
 Dameshek, W., 53, 66, 69
 Datesman, R. W., 21
 Daughaday, W. H., 87
 Davidson, C. S., 101, 110, 111
 Davis, J. O., 92
 Davison, J. P., 43
 Davison, M. M., 24
 Davolos, D., 16
 Deane, N., 101
 DeGraff, A. C., 23
 de Lappe, G. W., 28
 De Kruif, D., 28
 Delisle, C., 82
 Dell, E., 20
 Denham, S. W., 50
 Dennis, E. W., 3
 Denton, J., 111
 de Venanzi, F., 88
 Dexter, L., 73
 Dickes, R., 53
 Doane, J. H., Jr., 81
 Dobyns, B., 94
 Dodd, M. C., 3
 Doig, R. K., 46
 Donegan, C. C., 64
 Doolan, P. D., 44, 89
 Dowling, H. F., 11, 100, 104
 Doyle, J. T., 39
 Drake, M., 58
 Drucker, W. R., 9
 DuBois, E. L., 30
 Duff, I. F., 3
 Duffy, B. J., Jr., 56
 Duggan, J. J., 53
 Duryee, A. W., 16
 Dustan, H. P., 6
 Eadie, G. S., 91

 Eckhardt, R. D., 101
 Edelman, I. S., 56
 Edson, J. N., 53
 Eisenberg, G. M., 103
 Eisenberg, S., 77
 Elden, H., 42
 Elkinton, J. R., 107
 Ellis, L. B., 17
 Ellison, R. R., 52, 66
 Elmlinger, P. J., 61
 El-Rawi, I., 31
 Engel, F. L., 46
 Engle, R. L., Jr., 62
 Engstrom, R. M., 80
 Epstein, B., 17
 Epstein, F. H., 76
 Erdman, L. A., 96
 Erickson, R. J., 102
 Ersler, I., 56
 Escher, G. C., 51

 Fajans, S. S., 89
 Faloon, W. W., 22
 Farber, E. M., 48
 Feinstein, B., 29
 Felsted, E. T., 35

 Feltes, J., 68
 Ferguson, Bruce, 111
 Ferguson, T. B., 76
 Field, J. B., 26, 70
 Finch, C. A., 66
 Finch, S. C., 13, 61
 Finkbeiner, J. A., 15, 39, 75
 Finnerty, F. A., Jr., 54
 Fisher, B., 4
 Fisher, B. M., 102
 Fisher, M. M., 16
 Fittipaldi, J. F., 78
 Fitzhugh, F. W., Jr., 39
 Flamm, G. H., 53
 Fletcher, G. H., 51
 Foraker, A. G., 50
 Ford, R. V., 10, 48, 106
 Forman, S., 40
 Forsham, P. H., 32
 Foster, W. J., 38
 Frank, N. R., 116
 Fraser, R., 76, 79
 Frawley, T. F., 102
 Frayser, K. R., 51
 Freis, E. D., 18, 54
 French, R., 29
 Friedberg, C. K., 19, 107
 Friedman, I. H., 75, 80
 Fuchs, B., 99
 Furman, R. H., 38, 40

 Gabuzda, G. J., Jr., 111
 Gaensler, E. A., 115, 116
 Gale, R. G., 40
 Gallagher, T. F., 89
 Gamble, J. F., 38
 Gardner, L. I., 93
 Gastineau, C. F., 20
 Geiger, E., 31
 Gendel, B. R., 5
 Giannini, M. J., 52
 Giges, B., 86
 Gilbert, R. P., 76, 80
 Gilder, H., 24
 Gilford, S. R., 79
 Gillespie, J. F., 18
 Ginsberg, V., 13, 52, 66
 Glass, G. B. J., 65
 Glendening, M. P., 29
 Glover, R. P., 19
 Goldberg, M. A., 76, 80
 Goldenberg, H., 66
 Goldfarb, M. S., 26, 70
 Goldman, M. A., 104
 Goldman, R., 35
 Golub, O. J., 36
 Goodale, W. T., 86
 Gotch, F. A., 32
 Gott, C. L., 51
 Grace, W. J., 62
 Graham, D., 20
 Green, R., 47
 Green, R. S., 16
 Gregory, J. B., 41
 Gregory, R., 40, 41
 Griffin, A. C., 33, 113
 Griffin, J., 80
 Griffith, G. C., 26, 70
 Grissom, R. L., 7, 8, 74
 Grollman, A., 42
 Grossberg, S., 42
 Gubner, R., 74
 Gutman, A. B., 107
 Gylfe, J., 23

 Hackel, D. B., 86
 Hahn, E. O., 4
 Hall, C., 41
 Hall, O., 41
 Halperin, M. H., 75
 Halpern, M., 82
 Hamrick, L. W., Jr., 43, 46
 Handley, C. A., 48
 Hansen, R. W., 98
 Harden, G., 91
 Harper, O. F., Jr., 105
 Harrison, S., 84
 Hatcher, J. D., 75
 Haynes, F. W., 73
 Heinrich, C., 6
 Hellems, H. K., 6, 63
 Heller, P., 69
 Hellman, L., 89
 Helmer, O. M., 87
 Henle, W., 58
 Henry, R. J., 36
 Hettig, R. A., 38
 Hetzel, B. S., 85
 Heyman, A., 83
 Hickam, J. B., 39, 51
 Hinds, D. B., 51
 Hinkle, L. E., Jr., 1, 85, 97, 106
 Hirsch, B. B., 18
 Hodgson, P. E., 3
 Hollander, F., 98
 Hollander, W., 75, 80
 Holmes, J. H., 11
 Holmes, T. H., 101
 Hopper, J., Jr., 23
 Houser, H. B., 72
 Howard, R. P., 94
 Howell, D. S., 92
 Howell, W. L., 16
 Hufnagle, C. A., 18
 Hughes, R. H., 11
 Hui, K. K. L., 59
 Hull, H. B., 8
 Humoller, F. L., 104
 Hurd, E. L., 23
 Hurst, W. R., 90
 Huston, E. S., 7
 Huth, E. J., 17, 107

 Inkley, S., 77
 Innerfeld, I., 22, 59
 Iseri, L. T., 56
 Island, D., 32
 Israel, H. L., 85
 Ivers, J. B., 41

 Jackson, G. G., 100, 104
 Jacobsen, G. J., 36
 Jacox, R. F., 13
 Jahn, J. P., 34, 102
 Jahnke, E. S., Jr., 112
 James, A. H., 56
 James, G. W., III, 14, 64
 James, J. A., 108
 Janowitz, H. D., 98
 Jefferies, W. McK., 9, 94
 Jenkins, D. E., 47
 Jenkins, L., 29
 Johnson, B. B., 93
 Johnson, J. B., 17
 Johnson, P. C., 10, 95
 Johnson, S. A., 64
 Jones, F. L., 49
 Jones, P. O., 47
 Joseph, N. R., 8
 Judson, W., 75, 80

- Kaine, H. D., 89
 Kaplan, E., 63
 Karmen, A., 90
 Katine, F., 23
 Katz, S., 103
 Kawata, N., 104
 Keitel, H. G., 77
 Keller, D. H., 17
 Kelly, F. J., 113
 Kelly, K. H., 69
 Kelly, L. W., Jr., 94
 Kerby, G. P., 91
 Kibler, R. F., 44, 109
 Kinsell, L. W., 34, 36, 102
 Kirtley, W. R., 87
 Kleeman, C. R., 85
 Klingensmith, W. H., 105
 Klopp, C. T., 22
 Kobayashi, M., 40, 41
 Kofman, S., 100
 Kolb, F. O., 32
 Komesu, S., 6
 Komorov, S. A., 57
 Kowalski, H. J., 17, 78
 Kramer, P., 75
 Krieger, H., 77
 Kroop, I. G., 54
 Kunkle, E. C., 43
 Kupperman, H. S., 23
 Kyle, L. H., 44, 89, 96

 LaDue, J. S., 15, 39, 71, 72, 75, 90
 Lange, J., 28
 Langton, J., 29
 Lasser, R. P., 17
 Lau, F. Y., 29
 Lawrence, J. H., 61
 Learner, N., 81
 Leavell, B. S., 64
 Lee, P., 20
 Lee, R. E., 55
 Lehdorff, H., 52
 Leight, L., 6, 63
 Leiter, L., 91
 Lemon, H. M., 24, 25, 84
 Lepper, M. H., 11, 100, 104
 Levy, S., 9, 87
 Levin, W. C., 90
 Levine, B., 114
 Levinsky, W. J., 90
 Levy, R. P., 94
 Lewis, L., 84
 Lewis, L. A., 3
 Libby, R., 37
 Lichtman, H. C., 13, 66
 Liddle, G. W., 32
 Lillick, L. C., 65
 Limarzi, L. R., 4
 Lindgren, I., 115, 116
 Lindsay, S., 32
 Littman, A. M., 69
 Littman, M. L., 57
 Livesay, W. R., 7, 41, 48, 81
 Lloyd, N., 36
 Loewe, L., 17
 Longabough, E. E., 95
 Looney, J. M., 84
 Lorber, S. H., 21, 57
 Louis, L. H., 89
 Love, V. L., 53
 Love, W. D., 45
 Lowenstein, B. E., 82
 Lowman, E. W., 20
 Lowmore, B. S., 94
 Lucas, J. E., 109

 Luetscher, J. A., 93
 Luhby, A. L., 52, 57
 Lukas, D. S., 15, 79, 85
 Lyons, R. H., 53

 McColl, C. A., 96
 McCord, M. C., 6, 28
 McCormick, G., 103
 McCroan, J. E., 97
 McDonald, L., 73, 74
 McGowan, J., 98
 McIntosh, H. D., 39
 McIntosh, H. W., 35
 McIver, C., 35
 McKinney, G. R., 47
 Madison, L. L., 43
 Maisel, B., 59
 Malamut, L. L., 58
 Mandel, E. E., 45, 49
 March, J., 7
 Marshall, E., 103
 Martin, F. E., 12, 116
 Martin, S. P., 47
 Master, A. M., 54
 Mather, R. W., 84
 May, L. G., 40, 41
 Mead, J., 115, 116
 Meagher, T. R., 34, 102
 Megibow, R. S., 18
 Meneely, G. R., 40
 Menon, P. O., 100
 Merideth, A. M., 100
 Meroney, W. H., 86
 Messite, J., 66
 Metcalf, J., 108
 Meyers, W. P. L., 20
 Michaels, G. D., 36
 Middlebrook, J., 116
 Miller, G., 68
 Miller, M., 9, 87
 Miller, S. L., 7
 Miller, S. T., 81
 Minor, J., 107
 Molander, D. W., 110
 Montgomery, M. M., 8
 Monto, R. W., 65
 Moore, F. D., 56
 Moore, J. E., 111, 14
 Morgan, C. F., 16
 Morgan, F. M., 36
 Moser, M., 54
 Motulsky, A. G., 64, 71, 100
 Moyer, J. H., 7, 42, 47, 48, 81, 106
 Mueller, R. P., 94
 Murphy, J. R., 87
 Murphy, Q. R., 81
 Mushet, C. W., 14
 Myers, G. H., 116
 Myers, J. D., 44, 46, 109

 Neel, J. V., 62, 63
 Nelson, D. H., 93
 Neubauer, R. A., 23, 58
 Nichols, G., Jr., 77, 91
 Nichols, N., 77, 91
 Nicholson, E., 31
 Noll, J. W., 22

 O'Brien, G., 81
 O'Brien, W. A., Jr., 67
 Omsted, L. W., 115
 Olsen, L., 29
 Olson, R. E., 86
 Olwin, J. H., 71
 O'Neal, M., 113

 O'Neill, T. J. E., 19
 Oppenheimer, M. J., 1
 Osawa, E., 36
 Osher, H., 75
 Ottoman, R. E., 30
 Owen, J. A., Jr., 45
 Owings, R. H., 112

 Page, E. W., 29
 Page, I. H., 6
 Palmer, E. D., 112
 Palmer, R. A., 35
 Parker, F., Jr., 110
 Parker, R. T., 100
 Parrish, A. E., 88
 Parson, W., 44, 45, 88, 91
 Partenope, E. A., 79
 Partridge, J. W., 34
 Pascale, L. R., 7, 71, 74
 Patterson, J. L., Jr., 39, 83
 Paul, J. T., 4
 Paul, M., 71
 Pelner, L., 19, 24
 Perle, G., 24
 Perry, W. D., 34, 97
 Perry, W. P., 4
 Persky, L., 5
 Petersdorf, R. G., 49
 Petersen, H. H., 34, 102
 Petrakis, N. L., 26
 Pfeiffer, J. B., Jr., 43
 Phillips, G. B., 110
 Plough, I. C., 101
 Plummer, K., 21, 99
 Plummer, N., 97
 Pordy, L., 54
 Porter, R. R., 58
 Powell, J., 98
 Power, M. H., 20
 Pressman, R. S., 105
 Princiotta, J. V., 16
 Prior, J. T., 22

 Quinn, M., 85

 Rabinowitz, M., 73, 74
 Rammelkamp, C. H., Jr., 4
 Ramsay, G. D., 70
 Rath, C. E., 62
 Rebuck, J. W., 65
 Redisch, W., 82
 Reicher, N. B., 59
 Reifenstein, E. C., Jr., 94
 Reifenstein, G. H., 58
 Reifenstein, R. W., 101
 Reilly, W. A., 29
 Reisner, E. H., Jr., 14
 Reynolds, W. E., 101
 Rich, M., 42
 Rinfret, A. P., 32, 33, 113
 Rinzler, S. H., 18, 54
 Ritts, R. E., 22, 103
 Robertson, C. R., 113
 Robinson, J., 13
 Roche, M., 88
 Rohn, R. J., 8
 Romansky, M. J., 22, 103
 Rosch, P. J., 102
 Rose, J. C., 18, 62, 79
 Rosecan, M., 87
 Rosenberg, M. L., 35
 Rosenfeld, R., 89
 Rosenfeld, S., 18
 Rosenthal, M. C., 66
 Rosenthal, R. L., 18

- Rosevear, J., 76
 Ross, J. F., 13, 20, 61, 111
 Rothchild, I., 10
 Rowe, G. G., 81
 Rubin, G., 91
 Ruegamer, W., 11
 Ruegsegger, P., 71
 Rundles, R. W., 114
 Ruskin, A., 41
 Ruskin, B., 41
 Russell, W. O., 51

 Sandberg, A. A., 93
 Sanneman, E. H., 3
 Saslaw, M. S., 42
 Saxton, G. A., Jr., 116
 Sborov, V. M., 86, 101, 112
 Scaparone, M., 104
 Schaaf, M., 96
 Schack, J. A., 55
 Scherbel, A. L., 84
 Schiess, W. A., 56
 Schieve, J. F., 8
 Schiller, F., 29
 Schneider, C. L., 80
 Schneider, R. G., 62
 Schoen, A. M., 46
 Schoen, I., 33
 Schottstaedt, W. W., 106
 Schwartz, R., 111
 Scott, K. G., 29
 Scribner, B. H., 109
 Sedwitz, J., 22
 Seed, L., 4
 Segalove, M., 36
 Seldin, D. W., 45, 92
 Seligson, D., 86
 Selverstone, L. A., 7, 74
 Sensenbach, W., 43
 Seven, M., 103
 Shaffer, A., 73
 Shapiro, A. P., 42
 Shapiro, H. D., 15
 Sharon, W. S., 112
 Shay, H., 21, 57
 Shean, R., 82
 Shimkin, M. B., 114
 Shulman, N. R., 68
 Shuman, C. R., 78, 81, 84
 Sidbury, J. B., Jr., 45
 Siegel, A. C., 30, 34, 97
 Silber, E. N., 73
 Simonson, E., 7
 Singer, K., 4, 64
 Siple, H., 57
 Sirola, J. H., 107
 Sisson, J. H., 31
 Skeels, R. F., 33
 Slater, S. R., 54
 Sleisenger, M. H., 24
 Smith, C. W., 101

 Smith, L. A., 112
 Smith, R. W., Jr., 96
 Smith, V., 64
 Smyth, N. P. D., 33, 34, 95
 Snider, H., 6
 Snider, T. H., 63
 Snyder, H., 7
 Snyder, H. B., 42, 81
 Snyder, M. J., 100
 Sokolow, M., 28
 Soler, A., 79
 Soloff, L. A., 19, 75
 Solomon, A. K., 113
 Sones, M., 85
 Soper, H. A., 101
 Spaet, T. H., 27, 70
 Spies, H. W., 11
 Sprinkle, P., 44
 Spurr, C. L., 10, 48, 106, 109
 Squires, R. D., 17, 107
 Stahlman, M. T., 40
 Stanley, M. M., 98
 Starr, L. E., 97
 Starr, P., 36, 70
 Stead, W. W., 12, 116
 Steck, I. E., 8
 Steele, J. M., 82
 Stefanini, M., 5, 52, 69
 Steinbach, H. L., 32
 Steinberg, I., 15
 Sternberg, W. N., 48
 Stirrett, L. A., 37
 Stohlman, F., Jr., 62, 67
 Stokes, J., Jr., 58
 Stolzer, B. L., 72
 Storey, P., 103
 Sutherland, C. G., 49
 Swisher, S. N., Jr., 67
 Szilagyi, D. E., 33, 34, 95

 Tannenbaum, O., 55
 Taylor, R. D., 6
 Taymor, R. C., 19, 54, 107
 Teschan, P. E., 108
 Thill, A. E., 102
 Thompson, J., 25
 Tobian, L., Jr., 79
 Travell, J., 18
 Tsumagari, Y., 43
 Tunis, M. M., 55, 82
 Turner, H. H., 94
 Turner, R., 78
 Tyler, F. H., 93

 Uroblewski, F., 39

 Vanderlinde, R. J., 113
 Vera, J., 88
 Vesell, H., 55
 Vetne, G., 64

 Viranuvatti, V., 56
 Vose, S., 25

 Waife, S. O., 87
 Waldman, S., 19, 24
 Waldstein, S. S., 86
 Walser, M., 45, 92
 Walsh, J. R., 9, 69
 Wang, C., 89
 Wannamaker, L. W., 34, 97
 Ward, G., 27
 Ward, M. K., 97
 Ware, A. G., 26, 70
 Watson, R. J., 13, 15, 52, 66
 Wedell, W., 29
 Weiner, L., 14
 Weisberger, A. S., 5, 114
 Weisinger, B. B., III, 99
 Weiss, W., 103
 Welham, W. C., 44, 89
 Welt, I. D., 113
 Welt, L. G., 49
 Werk, E. E., Jr., 46
 Wertheimer, L., 82
 Wessler, S., 72
 Westlake, R. E., 56
 Wexler, B. C., 33
 Wharton, G. K., 36
 White, A. G., 91
 White, L. P., 27, 69, 114
 Whitrock, R. M., 98
 Whittenberger, J. L., 115, 116
 Wilhoit, W. M., 43
 Williams, H. R., 97
 Wilson, W. L., 38
 Winkelstein, A., 98
 Wissler, R. W., 26
 Wohl, M., 78
 Wolf, S., 46, 117
 Wolff, H. G., 46, 55, 79, 82, 85, 106
 Wolfson, W. Q., 62
 Woodward, H., 9, 87
 Woodward, T. E., 100
 Wotiz, H., 25
 Wright, C.-S., 4
 Wright, L. D., 23
 Wroblewski, F., 15, 71, 72, 75, 90
 Wynne, E. S., 51

 Young, L. E., 67
 Yow, E. M., 47
 Yu, T. F., 107
 Yuhl, E. T., 37

 Zahn, D., 101
 Zatuchni, J., 19, 75
 Zimmerman, H. J., 9, 69, 104
 Zinsser, H. H., 36
 Zivin, S., 8
 Zuelzer, W. W., 63

SUBJECT INDEX

- Abstracts**, preparation of, editorial, 118
- Acid-base balance**
in Cushing's syndrome, 45
disturbances of, and sodium and chloride balances 20
in uremia during hemodialysis, 108
- ACTH**
and blood volume and fluid volume, 92
-cortisone therapy for infections and toxemias, 34
effect on total body fat, 89
increased responsiveness to, 32
and other pituitary-adrenal factor, 33
and rheumatic carditis, 72
in severe infections, 102
- Actinomycosis**, pulmonary, and chloromycetin, 57
- Adrenal**
corticosteroids, and sodium and potassium excretion, 93
insufficiency, relative, 93
steroids in liver disease, 24
- Adrenocortical function**
evaluating level, 33
and isonicotinic acid hydrazide therapy, 102
and tuberculosis, 101
- Alcoholism**, and the liver, 110
- Allergy**, and Collagen Diseases, *see* Collagen Diseases and Allergy
- Alveolar-capillary membrane**, oxygen diffusion capacity in mitral stenosis, 6
- Aminophyllin**, in acute myocardial infarction, 80
- Amyl nitrite**, and headache, 82
- Anemia**
auto-immune hemolytic, of malignant lymphocytic disease, 66
hypoplastic, and Cortisone therapy, 38
iron deficiency, severe in adolescent male, 62
megaloblastic
cell survival in, 64
dynamics of erythropoiesis in, 64
use of citrovorum factor in, 66
pernicious
and intrinsic factor concentrate from hog stomach mucosa, 65
prothrombin concentration in, 64
treated with vitamin B₁₂, 64, 65
B₁₂ in blood and urine, 65
of portal cirrhosis, 111
sickle cell, 4
hemodynamic studies in, 63
and multiple whole blood transfusions, 64
splenic, observations on mechanism of, 66
- Angina**, effect of heparin on, 18
pectoris, and esophageal and anginal pain, 75
- Angiotonin**, and pulmonary and systemic arterial pressure, 40
- Anoxemic polycythemia**, humoral mechanism for, 62
- Antibiotic(s)**, 11, 22-23, 34-35, 47-48, 57-60, 100-106
therapy, for infections and toxemias, 34
- Antibody**, production in rheumatic fever, 4
- Anticholinergic agents** in gastric secretion, 98
- Anticoagulant**
Dipaxin, a new oral, 71
a new indandione, 26
phenylindandione, 3
studies, and a new synthetic heparinoid, 70
therapy for myocardial infarction, 40
- Anion-cation exchange resin**, for hepatic cirrhosis, 50
- Antidiuresis** in cirrhosis, 111
- Antidiuretic hormone**, in hepatic and cardiac disease, 91
- Apresoline**, renal vascular response to, 6
- Aramine**, in renal hemodynamics, 48
- Arterial pressure**, 40
and six drugs, 82
and vascular responses of the kidney, 82
- Arteriovenous fistula**, and red cell, plasma, and total blood volume, 76
- Atherosclerosis**
and deproteinated pancreatic extract, 16
effect of post-heparin plasma on optical density of emulsions in, 38
- Ascites**, and DCA and cortisone, 92
- Ascitic fluid**, and penicillin, 104
- Aspirin**, and rheumatic carditis, 72
- Aureomycin**
and liver enzyme system, 104
and liver function tests, 57
and nitrogen metabolism and liver histology, 22
- Auricular arrhythmias**, and hyperthyroidism, 94
- Auricular fibrillation**
hyperactive carotid sinus in, 75
surgery for, 15, 39, 75
- Auscultatory sphygmomanometric method**, defects in, 42
- Azotemia**, studies on, 49
- Bacteria**, effect on leukocytes, 47
- Ballistocardiogram**, ventricular complex in, 55
- Ballistocardiograph**
apparatus, dual displacement and velocity, 54
low frequency, and the cold pressor test, 79
- Ballistocardiography**
problems encountered in, 28
tridirectional, 53
- Banthine**, and gastric and pancreatic secretion, 98
- Basophils**, a simple method of counting, 14
- Benemid (probenecid)**
metabolic effects of, 10
renal effects of, 10
- Benzoate**, and rheumatic disorders and collagen diseases, 84
- Blood**, 3-6, 13-15, 26-27, 38-39, 52-53, 61-72
anti-rabbit cell factors in, 14
cells, *see* Blood cells
clotting, effect of paritol on, 38
immunologic mechanisms of leukocyte abnormalities, 13
leukemic, and activity of mature granulocytes, 68
level, and sulfonamide, 105
oxygen, and cerebral circulation, 83
pressure,
arterial, influenced by hypoxemia, 39
and changes in cerebrospinal fluid pressure, 82
recorded by a new instrument, 79
thrombopenic factor in, 69
transfusion, of whole blood in sickle cell anemia, 64
volume
and ACTH and cortisone, 92
in anemia of portal cirrhosis, 111
determined by use of Cr⁵¹, 29
plasma
and arteriovenous fistula, 76
and I¹³¹ and T-1824, 77
red cell, and arteriovenous fistula, 76
- Blood cell(s)**,
red
and arteriovenous fistula, 76
life span of, 61
in hereditary ovalocytosis, 64
potassium, in diabetic acidosis, 77
sickle cell hemoglobins within, 4
white
abnormalities, mechanisms of, 13
and bacterial products and hormones, 47
intravascular life of, 27
- Body composition**, measurement of, 44
- Body fat**
and ACTH, 89
measurement of, 89

- Bone marrow**
in lymphocytic leukemia, 114
normal and leukemic pressure of, 26
- Bone matrix**, measurement of penetration of sodium and water in, 56
- Bone sodium**, availability of, 91
- Bromsulphalein test**, in cirrhosis, 110
- Bronchogenic carcinoma**, and nitrogen mustard therapy, 114
- Butazolidine**, for rheumatoid arthritis, 20
- Calcium infusion technic**, and parathyroid function, 96
- Calcium serum changes** in pancreatitis, 11
- Cancer**
advanced mammary, dihydrotestosterone therapy for, 51
disseminated nonprostatic, serum acid phosphatase in, 25
liver, and pituitary hormones, 113
metastatic, diagnosis of, 37
and *vibrio metschnikovii* vaccine, 51
- Canicola fever**, water-borne outbreak of, 97
- Carbohydrate**
and insulin treatment, 87
metabolism, and HGF, Glukagon, 87
- Carbomycin**, and clinical pharmacology, 104
- Carbon dioxide**, and cerebral circulation, 83
- Carcinoma**, see Cancer
- Cardiac**
catheterization, and Eisenmenger complex, 73
disease
and antidiuretic hormone, 91
and water retention, 91
efficiency, and hexamethonium bromide, 81
output
in chronic disease of liver, 17
and cold pressor test, 79
with compression of interrenal inferior vena cava, 41
work, and hexamethonium bromide, 81
- Cardiovascular system**, 6-7, 15-19, 28-29, 39-43, 53-56, 72-82
changes with arteriovenous fistulas, 15
dynamics, in acute uremia, 108
and renal disease, 17
- Carditis**, rheumatic, effects of cortisone, 54
and ACTH and aspirin, 72
- Carotid sinus**
in auricular fibrillation, 75
reflex, and changes in cerebrospinal fluid pressure, 82
- Cell growth**, and succinic dehydrogenase activity, 50
- Central nervous system**, 8, 29, 43, 82-84
- Cerebral circulation**, and blood oxygen and carbon dioxide, 83
- Cerebral metabolism**, normal values for, 43
- Cerebrospinal fluid**
electrolytes, and serum electrolytes, 83
and penicillin, 104
and electrocardiogram, blood pressure, pulse and carotid sinus reflex, 82
during experimental metabolic alkalosis, 7
- Chloride balance**, in electrolyte and acid-base disturbances, 20
- Chloromycetin**, for pulmonary actinomycosis, 57
- Cholesterol**
and deproteinated pancreatic extract, 16
metabolism, in normo- and hypercholesterolemic man, 89
- Circulatory system**, and norepinephrine, 6
see also Cardiovascular system
- Cirrhosis**
and antidiuresis and hyponatremia, 111
and esophageal varices and spider angiomas, 112
and flocculation and bromsulphalein tests, 110
portal, and blood volume and anemia, 111
- Citrovorum factor**, in pernicious anemia, 66
- Coagulation**, intravascular, and dicumarol and heparin, 72
- Cold pressor test**, and changes in cardiac output, 79
- Collagen disease and allergy**, 8-9, 20, 30-31, 84-85
and benzoate, 84
and serum glycine response, 84
- Complement-fixing antigen**, and herpes simplex, 101
- Compound F** (dehydrocortisone acetate), and joint and potential temperature in rheumatoid arthritis, 8
- Conglutinin**, and nature of serum enhancement of canine isohemagglutin, 6
- Coronary**
artery disorders, new diagnostic tests for, 54
flow, and hexamethonium bromide, 81
- Cor pulmonale**, acute, and pulmonary vascular occlusions, 80
- Corticoid metabolism**
and HGF, Glukagon, 87
urinary, and sodium and potassium excretion, 93
- Cortisone**
-ACTH-antibiotic therapy, and infections and toxemias, 34
and blood volume and fluid volume, 92
and diphtheria, 92
and electrolyte excretion in ascites, 92
and fatty liver changes, 23
for "fibrinolytic purpura," 5
and hypoplastic anemia, 38
and infections, 102
and nephrotoxic action of DL-serine, 43
and nucleic acid changes, 92
and rheumatic carditis, 54, 72
- Creatine**
metabolism, in concurrent hyperthyroidism and myasthenia gravis, 96
- Creatinine**, renal excretion of, 49
- Cushing's syndrome**
and acid-base equilibrium, nitrogen and electrolyte metabolism, 45
and N¹⁵ glycine, 91
- DCA**, and electrolyte excretion in ascites, 92
- Dehydrocortisone acetate**, and rheumatoid arthritis, 8
- Detergents**, and intestinal digestion, 99
- Diabetes**
and glucose, 88
and insulin, 86
sensitivity, 88
and myocardial metabolism, 86
and potassium and phosphorus, 88
- Diabetic acidosis**
and glucose and fructose therapy, 87
and relationship of electrocardiogram to red cell potassium, 77
and water and electrolytes, 87
- Diabetic ketosis**, and insulin, 87
- Dialysis**, intestinal, 49
- Diamox**, oral, as diuretic agent in heart failure, 19
- Dicumarol**, effect on intravascular coagulation, 72
- Diet**
dilution studies in obesity, 45
and hepatic cirrhosis, 50
and renal conservation of potassium, 107
- Digitoxin**, and the electrocardiogram, 56
- Dihydrotestosterone therapy**, for advanced mammary carcinoma, 51
- Dipaxin**, a new oral anticoagulant, 71
- Diphtheria**, and cortisone, 92
- Disodium calcium ethylene diamine tetra-acetic acetate (CaEDTA)**, for lead poisoning, 45
- Diuresis**
and heart failure, 19
and nephrotic edema, 108
- DL-ethionine**, metabolic effect of, 114
- Ductus arteriosus**, with reverse flow, syndrome of, 15

- Duodenal amylase**, and pancreatic insufficiency, 99
- Duodenum and stomach**, intraluminal pressure studies of, 21
- Edema**, pulmonary, methylpolysiloxane for, 16
- Eisenmenger complex**, diagnosis of, 73
- Electrocardiogram**
and acute changes in cerebrospinal fluid pressure, 82
changes in hyperkalemia, 39
in diabetic acidosis, 77
effect of digitoxin on, 56
unipolar precordial T wave in normal subjects, 17
- Electrolytes**
disturbances, sodium and chloride balances in, 20
excretion
and ambulation and head-up tilting, 106
and DCA and cortisone, 92
diurnal variations in, 106
fat, changes in experimental pancreatitis, 11
and hexamethonium and ambulatory state in hypertension, 48
and pitressin, 107
and sodium amytal, 80
imbalance, in ureterocolostomy, 109
metabolism, in Cushing's syndrome, 45
serum, and cerebrospinal fluid electrolytes, 83
therapy, in chronic renal disease, 23
tissue, in heart failure, 77
- Electrophoresis**, paper of abnormal hemoglobins, 62, 71 and sickle cell disease, 62
- Electrophoretic**
analysis of proteins in body fluids, 112
patterns in rheumatoid arthritis, 84
- Electroshock**, and ocular pressure, 84
- Emphysema**, pulmonary
cardiodynamic studies of, 4
mechanics of, 115
- Emulsions**, optical density of, 38
- Endocarditis**, and penicillin, 105
- Endocrine gland(s)**, 9-11, 20, 31-34, 43-46, 56-57, 85-97
disorders
and carbohydrate and corticoid metabolism, 87
and HGF, Glukagon, 87
- Endotracheal pressure**, during thoracic surgery, 116
- Enzymes**, serum proteolytic differentiation of, 68
- Epidemiology and public health**, 97-98
- Epinephrine**, and pulmonary and systemic arterial pressures, 40
- Erythrocytes**, *see* Blood cells, red
- Erythromycin**, studies in, 20, 103
- Erythropoiesis**, effect of protein depletion on, 26
- Esophageal varices**, in cirrhosis, 112
- Esophagus**, left atrial pulsations of, 17
- Essential hyperlipemia**,
and diet, normal factors and serum lipids, 89
- Estradiol-cyclo-Pentylpropionate (ECP)**, clinical experiences with, 33
- Ethanol**, and metabolism, 86
- Ethyl alcohol** and external pancreatic secretion, 21
- Euthyroidism**
and the disposal of I^{131} -labeled thyroxine, 10, 95
tapazole to increase I^{131} in, 56
- Exophthalmos**, and X-ray treatment, 96
- Fibrinolysin**, influence on survival in vivo of various coagulation factors, 5
- "Fibrinolytic Purpura,"** and Cortisone, 5
- Fick methods**, and the cold pressor test, 79
- Flocculation test**, in cirrhosis, 110
- Fluid excretion**, diurnal variations in, 106
- Fluid volume**, and ACTH and cortisone, 92
- Fructose metabolism**, effect of stress on, 9
- Ganglion blocking agents**, in congestive heart failure, 81
- Gastric function**
in "decorticate" man with gastric fistula, 46
an improved method of measurement, 46
- Gastric secretion**
study of, 98
and anticholinergic agents, 98
and Banthine, 98
in insulin-induced hypoglycemia, 21
- Gastrointestinal System**, 11, 21, 46-47, 57, 98-99
- Glomerular filtration rate (GFR)**, estimation by single injection technic, 35
- Glucocorticoid activity**, in adrenocortical function, 33
- Glucose**
and fructose therapy for diabetic acidosis, 87
injection
in diabetes, 88
and potassium, 88
and serum inorganic phosphorus, 88
metabolism, effect of stress on, 9
production, effect of insulin on, 44
- Glutamic-oxaloacetic transaminase**, in human serum, 90
- Glycine**, N^{14} , in Cushing's syndrome, 91
- Haptene sensitization**, 30
- Headache**
and amyl nitrite, 82
and cerebrospinal fluid pulse wave contours, 82
"cluster" type, 43
and histamine, 82
and parenteral ergotamine, 82
vascular, cranial and conjunctival vessels in, 55
- Heart**
disease, rheumatic, and menstruation, 78
failure
congestive
and blood volume, 77
diuresis in, 19
ganglion blocking agents in, 81
and mercurial diuretics to prevent low-salt reactions, 19
and plasma volume, 76
and thiamine excretion, 78
failure
and insulin, 86
and myocardial metabolism, 86
and Riker 3588, effect on renal and cerebral hemodynamics, 42
tissue electrolytes in, 77
rate, recorded by a new instrument, 79
succinic dehydrogenase activity in hypertension, 41
see also Cardiovascular system
- Heat exposure**, and metabolic responses, 85
- Helium**, to measure residual air, 51
- Hematology**
and hemoglobin C trait, 63
and Polycythemia vera, 4
and sickle cell anemia treated by multiple whole blood transfusions, 64
and sickle cell-Hemoglobin C disease, 63
see also Blood
- Hemodialysis**
and acid-base balance, 108
in acute uremia, 108
and cardiovascular dynamics, 108
- Hemodynamics**
cardiorenal
in mitral stenosis, 75
and sodium amytal, 80
and hexamethonium bromide, 81
in hypertension, 81
and moderate exercise, 79
normal values for, 43
renal
as affected by aramine, 48
and hexamethonium and the ambulatory state in hypertension, 48
in sickle cell anemia, 63
- Hemoglobins**
abnormal
paper electrophoresis of, 62, 71
studies on, 4
C trait, characteristics of, 63
"homozygous" type III (c), report of a case, 27

Hemoglobins (*Cont'd*)

type S (sickle cell) and type F (alkali-resistant) in red cell population in sickle cell anemia, 4

Hemolysis, cobra venom studies on, 52

Hemolytic disease, and demonstration of erythrocyte-bound antibody, 68

Heparin

and cardiac pain of angina, 18
effect on intravascular coagulation, 72

and lysozyme, 91
and P³²-labeled phospholipid, 90

Hepatic

decompensation, and body potassium, 111

disease

and antidiuretic hormone, 91
and water retention, 91
insufficiency, and plasma antithrombin titer, 59

see also Liver

Hepatitis

and nitrogen balance, 101
and strenuous exercise, 101
viral, asymptomatic carrier state in, 58

Herpes simplex, complement-fixing antigen of, 101

Hexamethonium

bromide, and coronary flow, cardiac work and cardiac efficiency, 81

chloride for hypertension, 7

for hypertension, 54
and renal hemodynamics and water and electrolyte excretion in hypertension, 48

salts, in hypertension, 42

HGF *see* Hyperglycemic-glycogenolytic factor

Histamine

and headache, 82

test, in Pheochromocytoma, 56

Hormones, effect on leukocytes, 47

"Host factor," in human illness, 97

Hydrallazine, in hypertension, 42

Hydrogen ion, and metabolic alkalosis, 7

Hyperglycemic - glycogenolytic Factor (HGF, Glukagon)

and endocrine disorders, 87

and carbohydrate and corticoid metabolism, 87

Hyperkalemia, sodium and calcium in electrocardiographic changes of, 39

Hypertension

and hexamethonium, 7, 54

and hexamethonium bromide, 81

and hydrallazine and hexamethonium salts, 42

and nephrectomy, bilateral, 79

and nephrectomy, unilateral, 58

and pregnancy, 29

and renal hemodynamics and water and electrolyte excretion as affected by

hexamethonium and the ambulatory state, 48

and succinic dehydrogenase of heart, kidney and liver, 41

and vascular responses of the kidney, 82

veriloid in oil for, 16

Hyperthyroidism

and auricular arrhythmias, 94

and creatine metabolism, 96

and disposal of thyroxine (I¹³¹-labelled), 10, 95

and radioiodine uptake and protein-bound iodine, 20

Hypertonic sodium lactate, for renal disease, 58

Hypocapnia, and arterial blood pressure, 39

Hypoglycemia, insulin-induced, for testing cholinergic blockade of gastric secretion, 21

Hyponatremia, in cirrhosis, 111

Hypotension

acute, treated with l-norepinephrine, 41

orthostatic, clinical significance in, 39

Hypothyroidism, and renal function, 109

I¹³¹ see Radioiodine

Icterus index determination, critique on, 36

Ileostomies, and small intestinal function, 99

Immunology, and sarcoidosis, 85

Infectious diseases and antibiotics, *see* Antibiotics

Influenza virus, and platelet agglutination, 100

Insulin

with and without added carbohydrate, 81

in diabetes, 86

in diabetic ketosis, 87

in heart failure, 86

and myocardial metabolism, 86

and net splanchnic glucose production, 44

sensitivity, in diabetic and non-diabetic individuals, 88

Interarterial septal defect, and the right ventricle, 76

Intestinal dialysis, 49

Intestinal digestion, and detergent, 99

Intestinal function (small) in ileostomies, 99

Inulin, renal excretion of, 49

Ion exchange column, for measurement of sodium and potassium, 113

Iron metabolism, relationship of iron plasma to the kinetics of, 61

Isoantibodies, immune (canine), observations on the wide spectrum of, 67

Isohemagglutinin A (canine), nature of serum enhancement of, 67

Isoniazid (isonicotinic acid hydrazide)

and streptomycin in tuberculous pneumonia, 103

for tuberculous meningitis, 11

and tuberculous pneumonia, 103

Isonicotinic acid

and derivatives, for pulmonary tuberculosis, alone and combined with streptomycin, 47

therapy, and adrenal cortical function, 102

ITP, *see* Purpura, idiopathic thrombocytopenic

Ketosteroid, (17)

excretion, and testosterone, 94

plasma clearance of, 93

secretion, and T.C.P. in oil solution and aqueous suspension, 31

Kidney and urinary tract, 23, 35-36, 48-50, 58, 106-109

demonstration of specific respiratory enzymes in, 48

disease of

electrolyte therapy in, 23

urinary excretion of sodium in, 23

effect of probenecid (Benemid) on, 10

succinic dehydrogenase activity in hypertension, 41

vascular responses of, 82

"L.E." Phenomenon

in penicillin hypersensitivity and serum sickness, 9

produced by rabbit antileukocytic serum, 69

Lead poisoning, treated with disodium calcium ethylene diamine tetra-acetic acetate (CaEDTA), 45

Leukemia

and activity of mature granulocytes, 68

bone marrow pressure in, 26

lymphocytic

and bone marrow, 114

and triethylene melamine, 114

multiple myeloma in, 15

Leukocytes *see* Blood cells, white

Lipoid liver deposits, and deproteinized pancreatic extract, 16

Liver, 23-24, 36-37, 50, 58-59, 109-112

and alcoholism, 110

cancer, and pituitary hormones, 113

cardiac output in chronic disease of, 17

cirrhosis of, and anion-cation exchange resin, 50

damage, methionine metabolism with, 36

and diet, 50

disease

and aureomycin, 22

adrenal steroids in, 24

"replacement" versus "occupation" therapy, 24

- enzyme system, and aureomycin, 104
 extract therapy, 3
 fatty changes of, 23
 function
 and pancreatic HGF, 109
 and portocaval shunt, 112
 tests, and aureomycin, 57
 histology, in hepatic disease as affected by aureomycin, 22
 in hypertension, succinic dehydrogenase activity of, 41
- Lupus erythematosus**
 disseminated, and nitrogen mustards and triethylene melamine, 8
 systemic, 30
- Lymphocytic disease**, auto-immune hemolytic anemia of, 66
- Lymphoma**, as complicated by renal calculi, 5
- Lysozyme**, and heparin, 91
- Maximum tubular excretory capacity** for para-aminohippuric acid (TmPAH), estimation by single injection technic, 35
- Melanoma**, and radioactive iodine, 115
- Meningitis**, tuberculous, isonicotinic acid hydrazide for, 11
- Menstruation**, and rheumatic heart disease, 78
- Metabolic alkalosis**, and cerebrospinal fluid pressure, pH and respiration, 7
- Metabolism**
 disorders of, and exchangeable potassium content, 31
 and dl-ethionine, 114
 effects of ethanol on, 86
 during heat exposure, 85
 during stress, 85
see also Endocrine glands and metabolism
- Metastases**, cardiac, incidence and clinical manifestations of, 72
see also Cancer
- Methionine metabolism**, and hepatic damage, 36
- Methods**, 112-113
- Methylpolysiloxane**, for pulmonary edema, 16
- Microdrepanocytic disease**, with sickle cell trait and thalassemia minor, 3
- Mineralocorticoid activity**, in adrenocortical function, 33
- Mitral**
 commissurotomy and physiologic measurements, 74
 and reactivation of rheumatic fever, 19
 insufficiency syndrome, following posterior infarction, 74
 stenosis
 clinical and physiologic correlation in patients with, 7
 and measurement of pulmonary compliance and resistance, 116
 and mitral valvuloplasty, 75
 oxygen diffusion capacity of alveolar-capillary membrane in, 6
 valvular disease
 and pulmonary vascular resistance, 73
 stenotic, insufficient and mixed syndromes of, 74
 valvuloplasty, in mitral stenosis, 75
- Myasthenia gravis**, and creatine metabolism, 96
- Myeloma**, multiple, leukemic nature of, 15
- Myocardial infarction**
 acute, and aminophyllin, 80
 and anticoagulant therapy, 40
- Myocardial metabolism**
 in diabetes, and heart failure, 86
 and insulin, 86
- Myxedema**, and disposal of thyroxine (I^{131} -labelled), 10, 95
 primary, water tolerance test in, 44
- Neoplastic disease**, 24-25, 50-51, 59-60, 113-115
- Nephrectomy**, for hypertension, 58, 79
- Nephrotic edema**, and diuresis, 108
- Nitrogen**
 balance in hepatitis, 101
 metabolism
 in Cushing's syndrome, 45
 in hepatic disease as affected by aureomycin, 22
 mustard
 and bronchogenic carcinoma, 114
 for disseminated lupus erythematosus, 8
 radioactive, excretion of in Cushing's syndrome, 91
- Norepinephrine**
 circulatory system, and, 6
 and pulmonary and systemic arterial pressure, 40
- Nucleic acid**, and cortisone in diphtheria, 92
- Nucleophagocytosis**, produced by rabbit antileukocytic serum, 69
- Obesity**, studies in, 88
- Ocular pressure**, during electroshock, 84
- Osteomalacia**, skeletal lesions in, 32
- Ovalocytosis**, hereditary, and red cell life span, 64
- Pain**
 in angina pectoris, 75
 studies of, 29
- Pancreatic**
 extract, deproteinated, and cholesterol, atherosclerosis and lipid liver deposits, 16
 HGF, and liver function, 109
 insufficiency, and serum and duodenal amylase, 99
 secretion
 and Bantline, 98
 external, effect of ethyl alcohol on, 21
- Pancreatitis**
 and calcium serum, urine and fat electrolyte changes, 11
 serum alkaline phosphatase studies in, 57
- Pantothenic acid**, and probenecid, 23
- Parathyroid function**, and calcium infusion technic, 96
- Parenteral ergotamine**, and headache, 82
- Paritol**, and blood clotting, 38
- Penicillin**
 and cerebrospinal, pleural and ascitic fluid, 104
 and "group A" beta hemolytic streptococcal disease, 105
 "L.E." phenomenon in hypersensitivity to, 9
 and subacute bacterial endocarditis, 105
- Phenylindandione**, 3
- Pheochromocytoma**, histamine test for, 56
- Phospholipid**, and heparin, 90
- Pitressin**, and renal hemodynamics, water and electrolyte excretion, 107
- Pituitary**
 factors, 33
 hormones, and liver cancer, 113
- Placebo administration**, toxic effects of, 117
- Plasma**
 antithrombin titer, in hepatic insufficiency, 59
 beef, antihemophilic activity of, 70
 effect of oncotic pressure of, 49
 iron, in relation to the kinetics of iron metabolism, 61
 post-heparin, effect on optical density of emulsions, 38
 salicylate, and urate clearance, 107
 volume
 and arteriovenous fistula, 76
 and congestive failure, 76
 and I^{131} and T-1824, 77
- Platelet agglutination**, and influenza virus, 100
- Plethysmography**, digital, in peripheral vascular disease, 18
- Pneumonia**, tuberculous, and Isoniazid and streptomycin, 103
- Pneumoperitoneum**
 artificial, 40
 in preoperative preparation for portocaval vein anastomosis, 59
- Pleural fluid**, and penicillin, 104

- Poliomyelitis**, and respiratory secretion, 100
- Polycythemia vera**
total thyroidectomy in, 4
and triethylene melamine, 52
- Polymyxin B**, and renal function, 47
- Polyvinyl pyrrolidone**, and tuberculosis, 103
- Portocaval**
shunt, and liver function, 112
vein anastomosis, and preoperative pneumoperitoneum, 59
- Posterior infarction**, and mitral insufficiency, 74
- Potassium**
in diabetes, 88
exchange, in erythrocytes and plasma, 45
excretion, and corticosteroids and corticoids, 93
and glucose injection, 88
and hepatic decompensation, 111
Rb⁸⁶ and Cs¹³⁴ as tracers of, 44
renal conservation of, 107
spaces, measurement of, 113
- Pregnancy**
and hemolysis, 52
histochemical enzyme study of cervix in, 50
and hypertension, 29
late, and pulmonary vascular occlusions, 80
- Probenecid (Benemid)**
Metabolic effects of, 10
and pantothenic acid renal clearance by, 23
renal effects of, 10
- Protein(s)**
analyzed in human sera with cationic detergents, 13
depletion, and erythropoiesis, 26
electrophoretic analysis in body fluids, 112
metabolism, and thermal trauma, 90
- Proteolytic enzymes**, and respiratory secretion in poliomyelitis, 100
- Public health**, 97-98
- Pulmonary**
compliance and resistance, measurement of, 116
emphysema, cardiodynamic studies of, 40
mechanics, in emphysema, 115
pressure, 40
resection, and ventilation in the presence of acidosis, 12
tuberculosis, treatment of, 47
vascular occlusions
and late pregnancy, 80
resulting in acute cor pulmonale, 80
vascular resistance, and mitral valvular disease, 73
wedge pressure curves, observations on, 73
- Pulse**, and changes in cerebrospinal fluid pressure, 82
- Purpura**, idiopathic thrombocytopenic (ITP)
cerebral hemodynamics in heart failure, 42
- Rocky Mountain spotted fever**, and rickettsia rickettsii, 100
- RPF** see Renal plasma flow
- Sarcoidosis**, immunologic studies in, 85
- Serum**
acid phosphatase, in disseminated nonprostatic carcinoma, 24
albumin, and protein metabolism after thermal trauma, 90
alkaline phosphatase studies, in pancreatitis, 57
amylase, and pancreatic insufficiency, 99
cholinesterase
colorimetric determination of, its value in hepatic and biliary tract diseases, 24
factors in, 110
and glutamic-oxaloacetic transaminase, 90
glycine response, and rheumatic disorders and collagen diseases, 84
inorganic phosphorus
in diabetes, 88
and glucose injection, 88
lipid
and diet factors, 89
and essential hyperlipemia, 89
and hormonal factors, 89
and new synthetic heparinoid, 70
proteins, analysis of human in, 13
proteolytic enzymes, differentiation of, 63
sickness, "L.E." phenomenon in, 9
- Sickle cell(s)**
anemia, see Anemia
disease, and paper electrophoresis, 62
-hemoglobin C disease, clinical and hematologic characteristics of, 63
hemoglobins in red cell population in sickle cell anemia, 4
trait in microdrepanocytic disease, 3
- Sigmoid vein**, and reabsorption of urinary constituents, 35
- Skin responses**, in haptene sensitization, 30
- Sodium**
amylal, and cardiorenal hemodynamics, 80
balance, in electrolyte and acid-base disturbances, 20
excretion, and corticosteroids and corticoids, 93
para-aminosalicylate, and tuberculosis, 103
spaces, measurement of, 113
- Spatial vector analysis**, applied to early right ventricular preponderance, 7
- "acute" versus "chronic," 69
and selective sequestration of platelets by the spleen, 52
- Radiolodine (I¹³¹)**
and hyperthyroidism with auricular arrhythmias, 94
and malignant melanoma, 115
and R-E system physiology, 113
and thyroid autotransplants, 95
tracer study, 33
uptake, by thyroid remnant after subtotal thyroidectomy, 34
- R-E system**, physiology of, using I¹³¹, 113
- Renal**
calculi, complication of lymphoma, 5
conservation of potassium, and low potassium diet, 107
disease
and cardiovascular system, 17
and hypertonic sodium lactate, 58
excretion, of creatinine and inulin, 49
failure, excretion of phosphorus in, 35
function
and ambulation and head-up tilting, 106
and hypothyroidism, 109
and polymyxin B, 47
hemodynamics
and aramine, 48
and hexamethonium and the ambulatory state in hypertension, 48
and pitressin, 107
plasma flow (RPF), estimation by single injection technique, 35
see also Kidney
- Respiration**, in metabolic alkalosis, 7
- Respiratory**
center, mechanical substitute for, 116
enzymes, in kidney, 48
secretion, in acute poliomyelitis, 100
system, 12, 51, 115-117
residual air measured with helium, 51
- Rheumatic disorders**
and benzoate, 84
and glycine response, 84
- Rheumatic fever**
and antibody production, 4
prevention of, 30
reactivated by mitral commissurotomy, 19
- Rheumatoid arthritis**
butazolidine for, 20
and Compound F, 8
and electrophoretic patterns, 84
- Rickettsia rickettsii**, and Rocky Mountain spotted fever, 100
- Riker 3588** (diethyl-amino-ethyl-theophylline hydrochloride), effect on renal and

- Specific gravity technic**
for measurement of body composition, 44
in measuring body fat, 89
- Spider angiomas**, in cirrhosis, 112
- Splanchnic glucose production**
(net), effect of insulin on, 44
- Splanchnic ketone production**, and sodium octanoate infusion, 46
- Spleen**, in idiopathic thrombocytopenic purpura, 52
- Squamous carcinoma of cervix**, trichomonas infestations in, 59
- Stomach and duodenum**, intraluminal pressure studies of, 21
- Streptococcal disease**, and penicillin, 105
- Streptococcal infection**, and immunological response, 30
- Streptococci** (group A)
and contaminated blankets, 34
and environment, 97
- Streptomycin**, for pulmonary tuberculosis, 47
- Stress**
and metabolic changes, 85
and tuberculosis, 101
- Succinic dehydrogenase activity**, and cell growth, 50
- Sulfonamide**, and blood level, 105
- Susceptibility**, to illness in adult women, 97
- Tapazole**, to increase I^{131} concentration in euthyroidism, 56
- TCP** *see* testosterone cyclopentylpropionate
- Terramycin**, toxicity of, 22
- Testosterone**
conversion rate, pattern, significance and possible use of, 10
cyclopentyl-propionate, and 17-ketosteroid secretion, 31
(endogenous) inhibition, and exogenous testosterone esters, 94
propionate, for acute and chronic liver disease, 36
- Tetraethylammonium**, and pulmonary and systemic arterial pressure, 40
- Thalassemia**
major, extracorporeal defect in, 13
minor, in microdrepanocytic disease, 3
- Thermal trauma**, and protein metabolism, 90
- Thiamine excretion**, and congestive heart failure, 78
- Thoracic**
inferior caval constriction and DCA and cortisone, 92
and electrolyte excretion, 92
surgery, and endotracheal pressure, 116
- Thromboembolic control**, with a new hypoprothrombinemic agent, 70
- Thrombopenic factor**, in human blood, 69
- Thyroid**
activity, after cold exposure, 31
autotransplants, survival of, 33, 95
function, and thyrotropin, 94
and subtotal thyroidectomy, 95
- Thyroidectomy**
subtotal
and radioiodine (I^{131}) uptake by thyroid remnant, 34
total
in polycythemia vera, 4
with radioactive iodine, 115
- Thyroiditis**, granulomatous, studies in, 32
- Thyrotropin**, and thyroid function, 94
- Thyroxine disposal** in myxedema, euthyroidism and hyperthyroidism, 10, 95
- Tissue iron distribution**, in erythropoiesis after protein depletion, 26
- TmPAH**, *see* Maximum tubular excretory capacity for para-aminohippuric acid
- Trichomonas infestations**, in squamous carcinoma of cervix, 59
- Triscupid insufficiency**, hemodynamic pattern in, 28
- Triethylene melamine**
and bone marrow in lymphocytic leukemia, 114
for disseminated lupus erythematosus, 8
for polycythemia vera, 52
- Trypsin, intravenous**
and acute inflammatory reactions, 22
administration of, 71
- Tuberculosis**
chemotherapy of, 103
and stress and adrenocortical function, 101
- T wave**, in unipolar precordial electrocardiogram, 17
- Urate clearance**, and plasma salicylate, 107
- Uremia**
and acid-base balance, 108
acute
and cardiovascular-dynamics, 108
and hemodialysis, 108
- Ureterocolostomy**, and electrolyte imbalance, 109
- Urinary tract**, *see* kidney and urinary tract
- Urine**
changes in pancreatitis, 11
constituents, reabsorbed from the sigmoid, 35
and liver extract therapy, 3
- Urogram**, quantitative, 36
- Vascular**
disease, peripheral digital plethysmography in, 18
responses of the kidney to six drugs, 82
- Venomotor reactions**, a study of, 53
- Venous pressure**, peripheral, and exercise, blood volume, cardiac and pulmonary pressure, 28
- Ventricular**
function, mechanical, 18
hypertrophy, early right spatial vector analysis applied to, 7
- Veriloid in oil**, for hypertension, 16
- Vibrio metschnikovii vaccine**, and irradiated cancer, 51
- Vitamin B₁₂**
and pernicious anemia, 64, 65
in urine after liver extract therapy, 3
- Water**
excretion
and ambulation and head-up tilting, 106
and hexamethonium in ambulatory state in hypertension, 48
and pitressin, 107
and sodium amytal, 80
retention
in cardiac disease, 91
in hepatic disease, 91
- Water tolerance test**, in primary myxedema, 44
- X-Ray treatment**, in malignant exophthalmos, 96

at]

tal

li-

cs,

ro-

nd

om

tal

six

of,

and

me,

ary

tial

ied

, 16

and

act

l-up

am-

per-

nary

nant

2005-2006

